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Seminars in fetal and neonatal medicine delivery room emergencies

The few minutes that precede and follow birth are some of the most drastic and significant in terms of changes in physiology and possible lifelong consequences. Within a few seconds, the newborn has to shift from a state in which gas exchange occurs exclusively at the placenta, to the extra uterine environment where survival becomes entirely dependent on its own cardiorespiratory system. This requires a number of complex and perfectly coordinated changes that allow lung aeration and perfusion, and the establishment of extra uterine gas exchange and circulation. Amazingly, in most births these changes occur successfully and babies transition from fetal to neonatal life without problems. When this transition does not occur normally and medical interventions are not effective, there can be lifelong devastating consequences for the infant.

There are many maternal and fetal conditions that can interfere with this normal transition. Therefore, it is critical to recognize these problems early so preventive or corrective interventions can be implemented as quickly as possible to assure a normal adaptation.

The chapters in this issue of Seminars of Fetal and Neonatal Medicine address emergencies that can interfere with normal transition immediately after birth. They also describe some of the interventions that can support a normal transition and minimize the devastating consequences of severe perinatal asphyxia. These interventions require anticipation, coordination between different teams of providers, and the proper environment and equipment. Most importantly, it is essential to have a perinatal team that is experienced and skilled in the steps required to assist mother and infant during this critical period. It is interesting that because these emergencies are often unanticipated, the responsibility may fall in the hands of trainees who may not be the most experienced providers. One way of avoiding this is to have a seamless communication and coordination between obstetrical, anesthesiology and neonatal teams to anticipate and adequately prepare for such emergencies.

Although resuscitation of the newborn in the delivery room is a topic that is discussed frequently in the literature, many of the mechanisms involved in the transition from fetal to neonatal physiology have only been uncovered recently. As a result, this new knowledge is producing rapid changes in the way infants are managed immediately after birth.

The chapters in this issue discuss the most recent advances in this critical area of newborn care and are written by some of the leading researchers and clinicians in this field.

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Issues in cardiopulmonary transition at birth

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ABSTRACT

The transition from fetal to newborn life involves a complex series of physiological events that commences with lung aeration, which is thought to involve 3 mechanisms. Two mechanisms occur during labour, Na^+ reabsorption and fetal postural changes, and one occurs after birth due to pressure gradients generated by inspiration. However, only one of these mechanisms, fetal postural changes, involves the loss of liquid from the respiratory system. Both other mechanisms involve liquid being reabsorbed from the airways into lung tissue. While this stimulates an increase in pulmonary blood flow (PBF), in large quantities this liquid can adversely affect postnatal respiratory function. The increase in PBF (i) facilitates the onset of pulmonary gas exchange and (ii) allows pulmonary venous return to take over the role of providing preload for the left ventricle, a role played by umbilical venous return during fetal life. Thus, aerating the lung and increasing PBF before umbilical cord clamping (known as physiological based cord clamping), can avoid the loss of preload and reduction in cardiac output that normally accompanies immediate cord clamping.

1. Introduction

At birth, the remarkable ease at which most infants transition to newborn life belies the complexity of the physiological changes that are needed to survive after birth. Before birth, the lungs are liquid-filled and gas exchange occurs across the placenta. Pulmonary blood flow (PBF) is low and the majority of right ventricular output bypasses the lungs and flows through the ductus arteriosus (DA) to enter the descending aorta [1,2]. As much of this blood is then directed through the placenta, the right ventricle supplies the majority of blood flowing through the fetal gas exchange organ (placenta), just like it does in adults. Similarly, in the fetus, a large proportion of the blood returning from the placenta to the heart is shunted (through the ductus venosus and foramen ovale) directly into the left side of the heart, bypassing the right side and the lungs. As such, in the fetus, blood returning from the fetal gas exchange organ (placenta), provides much of the preload for the left ventricle, just like in the adult, which receives blood returning from the lungs [3].

Switching the site of gas exchange from the placenta to the lungs at birth, necessitates that the airways are cleared of liquid, to allow the entry of air, and that pulmonary vascular resistance (PVR) substantially decreases. The latter is necessary so that: (i) the entire output from the right ventricle can be redirected through the lungs to facilitate gas exchange and (ii) PBF substantially increases (~30 fold) so that it can replace umbilical venous return as the source of preload for the left ventricle [2]. These major physiological changes are critical for survival after birth and are triggered by the one event that cannot occur before birth, aeration of the lungs. Indeed, lung aeration at birth is not just important for allowing the onset of pulmonary gas exchange. It also triggers a sequence of inter-dependent physiological events, beginning with the increase in PBF, that initiates a major reorganisation of the fetal circulation into the adult phenotype, allowing the two circulations to separate [2].

2. The respiratory transition at birth

Before birth, airway liquid is secreted by the lung and plays a vital role in fetal lung growth and development by maintaining the lung in a distended state [4,5]. Increasing the degree of lung distension is a potent stimulus for fetal lung growth whereas a reduction in lung expansion causes fetal lung growth and development to cease [4,5]. However, at birth this liquid must be cleared from the airways to allow the entry of air and the onset of pulmonary gas exchange. To understand how airway liquid clearance can affect respiratory function after birth, it helps to recognise that the lung passes through two distinct phases before it starts to function like an adult lung [1]. During the first

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phase, the airways are liquid-filled which precludes pulmonary gas exchange and greatly increases airway resistance. During the second phase, the airways are cleared of liquid, allowing pulmonary gas exchange, but the liquid has shifted into lung tissue. This causes a form of pulmonary oedema, which likely plays a critical role of stimulating the increase in PBF (see below), but can also reduce respiratory function. While the first phase is usually quite short (30–60 s), the second phase is markedly longer (4–6hrs) and can potentially influence respiratory function well into the newborn period [1].

3. Phase 1: Airway liquid clearance and lung aeration at birth

The timing and mechanisms of airway liquid clearance are generally not well understood, with many still believing that airway liquid clearance simply results from Na^+ reabsorption induced by the stress of labour. However, up to three mechanisms are involved, with the primary mechanism in any one infant depending upon the timing and mode of delivery [1]. Two of these mechanisms are active during labour and the third is active after birth (see below). Some have argued that liquid clearance begins days to weeks before labour onset [6]. However, the evidence supporting this concept was obtained from animal experiments performed before the relationship between reduced amniotic fluid volumes and reduced lung liquid volumes was fully recognised [7,8]. Indeed, a common side effect of fetal surgery in sheep is amniotic fluid leakage, which may have interfered with the findings. We now know that the volume of fetal lung liquid present in the airways before birth varies considerably between individuals and largely depends on the available intra-uterine space [5]. Reducing this space, as occurs with reduced amniotic fluid volumes, reduces lung liquid volumes [7] and it is possible that other factors, such as the presence of a twin, may have a similar effect.

3.1. Airway liquid clearance before birth

Na^+ reabsorption can result from increased circulating fetal adrenaline levels, induced by the stress of labour (particularly during vaginal delivery of the head), which act on alveolar epithelial cells to stimulate Na^+ uptake from the lung lumen [6,9]. This reverses the osmotic gradient across the lung epithelium leading to liquid reabsorption from the airways. While this mechanism has been demonstrated experimentally, it is only present late in gestation and pharmacological doses of adrenaline are required [10–12]. As such, this mechanism is not active in preterm infants. Furthermore, despite the requirement for very high adrenaline levels, maximum re-absorption rates are ~3 orders of magnitude less than airway liquid clearance rates after birth [10–12] (see below). Thus, if airway liquid clearance occurred by Na^+ reabsorption alone, it would take hours before gas exchange could occur, adrenaline levels would have to be elevated throughout this time and preterm infants would not be able to aerate their lungs [1]. There is also much confusion over whether adrenaline levels are consistently increased during delivery and whether the mode of delivery influences adrenaline levels. While no difference in cord blood adrenaline levels were found between infants delivered vaginally or by caesarean section (CS), this reference [13] is commonly cited (incorrectly) as demonstrating that adrenaline levels are increased in vaginally delivered, compared to CS delivered, infants. In contrast, asphyxic and breech delivered infants had markedly elevated adrenaline levels [13]. The concept that airway liquid clearance is not dependent upon Na^+ reabsorption is consistent with the finding that Na^+ channel blockade (with amiloride) does not affect the extent or the spatial and temporal pattern of airway liquid clearance after birth [14].

Forces imposed on the infant during uterine contractions can also cause large volumes of liquid to exit the lungs via the nose and mouth [7]. Indeed, gushes of liquid from the nose and mouth can be observed upon delivery of the head, which likely results from increased dorso-ventral flexion of the fetal abdomen during uterine contractions [15]. Increased spinal flexion, increases abdominal pressure and elevates the diaphragm causing an increase in transpulmonary pressure and the loss of lung liquid via the trachea [7]. As the fetal respiratory system is highly compliant, only small increases in transpulmonary pressure are needed to lose large volumes of liquid [16]. However, the contribution of this mechanism to airway liquid clearance at birth, likely varies considerably between individuals. For instance, infants delivered vaginally and exposed to strong uterine contractions during a protracted labour, will likely lose large volumes of lung liquid via this mechanism [1]. On the other hand, infants delivered by elective CS without labour will lose little or no liquid via this mechanism. It is important to note that this mechanism of airway liquid loss, is the only mechanism whereby liquid is completely lost from the respiratory system following its clearance. Both other mechanisms (Na^+ reabsorption and inspiratory efforts, see below) involve the clearance of liquid into lung tissue, before it is eventually cleared from the tissue hours after birth [1]. As described below, the presence of this liquid in lung tissue has significant implications for respiratory function after birth.

3.2. Airway liquid clearance after birth

Phase contrast X-ray imaging studies Fig. 1 have demonstrated that, after birth, the pressure gradients generated by inspiration rapidly and efficiently clear the airways of liquid, resulting in full aeration within 3–5 breaths (< 30secs) in term newborns [17,18]. Indeed, the calculated rates of liquid clearance during inspiration are astonishingly large (~32 L/hr/kg) and explain why infants can rapidly initiate pulmonary gas exchange after birth, even in infants born by CS without labour [17,18]. The images show that the air/liquid interface moves distally through the airways in a stepwise manner with each inspiration, with little or no distal movement between breaths Fig. 1. Some proximal movement can occur between breaths, which likely results from liquid re-entry into the airways [17,18].

The pressure gradients driving liquid movement distally through the airways and across the distal airway wall are derived from inspiration, which reduces interstitial tissue pressures [17,18]. This results in a large hydrostatic pressure gradient between the tissue and airways causing liquid to move out of the airways into the surrounding lung tissue. Similar pressure gradients can be applied using positive pressure ventilation, producing a similar effect [14,19,20]. The initial resistance to moving air into the lung after birth is governed by the resistance to moving liquid through the airways and across the distal airway wall. As lung liquid has a viscosity that is ~100x greater than air, the initial resistance to moving air into the lung is ~100x greater than it is following lung aeration and rapidly decreases as the lung aerates [21] Fig. 2. Preterm infants have smaller airways and as the resistance increases exponentially (4th power) as the airway radius decreases, the initial resistance to moving liquid through the airways at the start of lung aeration should be significantly greater in preterm compared to term infants [21] Fig. 2. Similarly, as the surface area of the distal airways increases exponentially with increasing gestational age, preterm infants have a markedly reduced distal airway surface area, which must also increase the resistance for liquid movement into lung tissue. Despite this, it is recommended that at birth preterm infants are ventilated with starting pressures that are much lower than term infants [22].

The reduction in airway resistance during lung aeration follows an exponential function that is difficult to predict, resulting in large changes in respiratory mechanics on a breath-by-breath basis [21]. Thus, using intermittent positive pressure ventilation (iPPV) with a single set inflation pressure during lung aeration may initially produce small tidal volume changes, but result in very large tidal volumes following lung aeration. As such, it is difficult to understand why highly sophisticated ventilators that can monitor and respond to breath-by-breath changes in respiratory mechanics are commonly used in the NICU, but not in the delivery room. Indeed, respiratory mechanics have

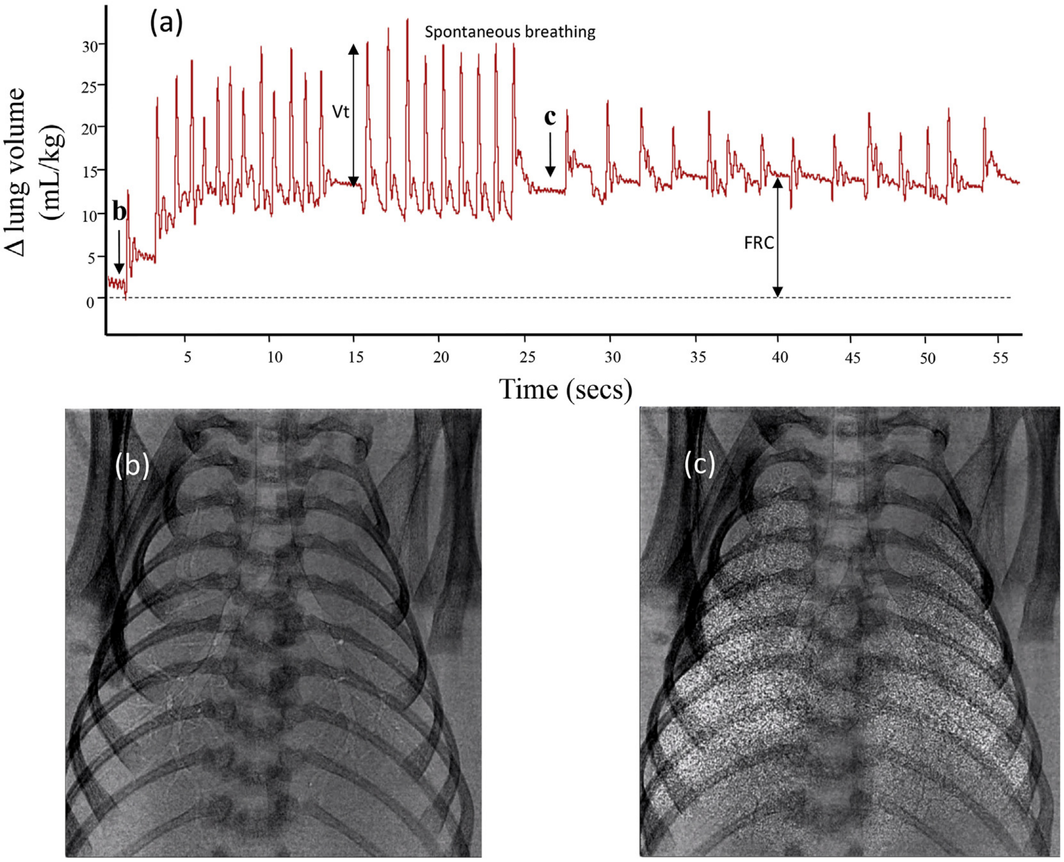

Fig. 1. (a) Lung gas volumes, measured by plethysmography, in spontaneously breathing near term newborn rabbits from birth. The increase in baseline volume represents the formation of a functional residual capacity (FRC), which rapidly increases with each breath. Initially, the tidal volumes are large (10–15 mL/kg), but decrease (to 7–8 mL/kg) following lung aeration. This newborn rabbit took ~15 s to generate an FRC of ~15 mL/kg (b) and (c) are phase contrast X-ray images, acquired at the time points indicated by (b) and (c) in the plethysmography recording (a), showing the degree of lung aeration at each time point. Data obtained from Ref. [17].

usually stabilised by the time the infant reaches the NICU, whereas in the delivery room, the changes in respiratory mechanics are rapid and complex. Despite this, ventilation in the delivery room most commonly involves the use of rudimentary devices (T-piece devices or resuscitation bags) that are incapable of automatically adjusting ventilation parameters to take into account rapidly changing respiratory mechanics. This likely greatly contributes to the large variation in tidal volumes measured in preterm infants at birth [23].

4. Phase 2: effect of airway liquid within lung tissue

As the lung's interstitial tissue compartment has a fixed volume, the entry of airway liquid into this compartment increases interstitial tissues pressures, causing a form of oedema that persists for 4–6 h while the liquid is gradually cleared from the tissue [24,25]. The presence of this liquid in lung tissue potentially has major implications for respiratory function after birth. For instance, as airway liquid is replaced with air when it moves into lung tissue, it still remains within the chest. As a result, the chest wall must expand to accommodate both the liquid and the volume of air that resides in the lung at end-expiration (functional residual capacity; FRC) [17] Fig. 3. The increase in interstitial tissue pressure also increases the pressure gradient for liquid to re-enter the airways at end-expiration, which is subsequently cleared during the next breath/inflation [18]. While the presence of this liquid in lung tissue also reduces lung compliance [26], making the lungs stiffer and more difficult to inflate, there is very little understanding for how this consequence of airway liquid clearance may contribute to respiratory morbidity in the new born.

4.1. *Transient tachypnea of the newborn*

Increased spinal flexion and airway liquid loss from the nose and mouth is the only mechanism of airway liquid clearance that results in the complete loss of liquid from the respiratory system [1]. Thus, if this mechanism is not activated, all liquid present in the airways at birth must be cleared (either by Na reabsorption or inspiration) across the distal airway wall into lung tissue. For example, in all infants born by elective CS without labour, the majority of airway liquid must be cleared by the pressures generated during inspiration and all of this liquid must enter lung tissue [1]. In contrast, infants delivered vaginally will have lost significant volumes of liquid via the nose and mouth during delivery [15]. As a result, after birth, the volume of liquid that must be cleared into lung tissue is considerably less. There is now mounting evidence to suggest that transient tachypnoea of the newborn (TTN) does not result from a failure to clear fetal lung liquid, but results from having larger volumes of airway liquid at the onset of breathing [1,26]. As a result, larger volumes must be cleared into lung tissue, which increases the degree of lung "oedema" following lung aeration [24,25]. This is consistent with the findings of multiple RCTs, targeting the stimulation of Na reabsorption mechanisms (eg β-agonists such as salbutamol), that have failed to show any benefit with regard to reducing the incidence or severity of TTN [27].

Recent experimental studies have simulated the influence of labour (reduced lung liquid) and absence of labour (increased lung liquid) on respiratory function and mechanics immediately after birth [26]. Increasing lung liquid volumes at birth, reduces lung compliance and FRC and causes the chest wall to expand further and the diaphragm to

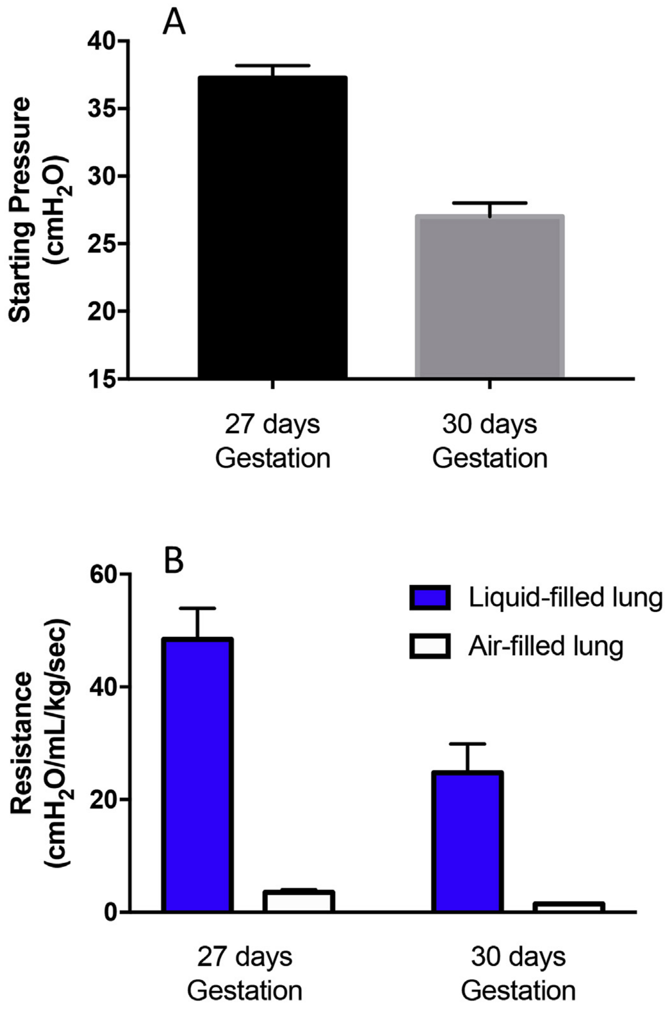

Fig. 2. (A) Inflation pressures required before gas first starts to move into the liquid-filled lung immediately after birth in either very premature (27 days gestational; black bar) or near-term (30 days gestation; grey bar) rabbits. The starting pressure is considerably less ($p < 0.001$) in older more mature newborn rabbits. (B) Airway resistance measured in a liquid-filled lung (blue bars) and moments later after lung aeration (open bar) in very premature (27 days gestation) and near-term (30 days gestion) newborn rabbits. Note that aeration of the lung markedly reduces airway resistance at both ages and that airway resistances are always less in older, more mature newborns. Data reploted from Ref. [21].

flatten [26]. These changes readily explain the respiratory symptoms characterised by infants diagnosed with TTN. The reduction in FRC explains the expiratory grunting, which is caused by closure of the glottis during expiration and is commonly used by newborns to preserve lung volumes (FRC) after birth. On the other hand, chest wall expansion and flattening of the diaphragm reduces inspiratory reserve volumes and when combined with a lower lung compliance, restricts tidal volumes. Thus, to sustain alveolar ventilation, respiratory rates must increase, which explains the tachypnea and laboured breathing.

With regard to understanding the causes and full significance of TTN, how it should be treated and whether it can be avoided in at risk infants, it is important to recognise that the diagnosis of TTN is imprecise, subjective and often occurs in retrospect after the infant has recovered [28]. As such, infants diagnosed with TTN are commonly regarded as a subgroup of near term infants with respiratory morbidity that is usually mild and self-limiting. Indeed, the latter characteristic is a significant contributing factor to the diagnosis, but it is highly questionable whether it has any clinical value with regard to treatment. It may also artificially divide infants into subgroups despite having the same underlying problem. Indeed, how should infants, who initially show similar TTN-like symptoms, but then develop more severe and protracted respiratory distress, be diagnosed? It is possible that the underlying morbidity is multifactorial that can progress from a mild respiratory disease into a major respiratory pathology (eg severe respiratory distress or pulmonary hypertension). The progression towards more severe disease may depend on factors such as the volume of airway liquid at the onset of breathing and the availability and timely use of treatments like continuous positive airway pressure (CPAP; see below) [29]. Indeed, accommodating large volumes of liquid in lung tissue may cause lung injury and respiratory distress due to a continuous cycle of airway liquid clearance and then re-entry with each breath [18]. As CPAP provides a positive pressure gradient that opposes liquid re-entry into the airways during expiration, this explains why CPAP may be an effective treatment for TTN [19,20]. However, prevention is better than treatment and so fully understanding the mechanism of TTN may help to develop delivery techniques at CS that simulate the liquid loss during vaginal delivery. Nevertheless, as language is important, it may be prudent to change the name or at the very least, remove the word “transient” as it is potentially misleading and necessitates that the diagnosis be made retrospectively.

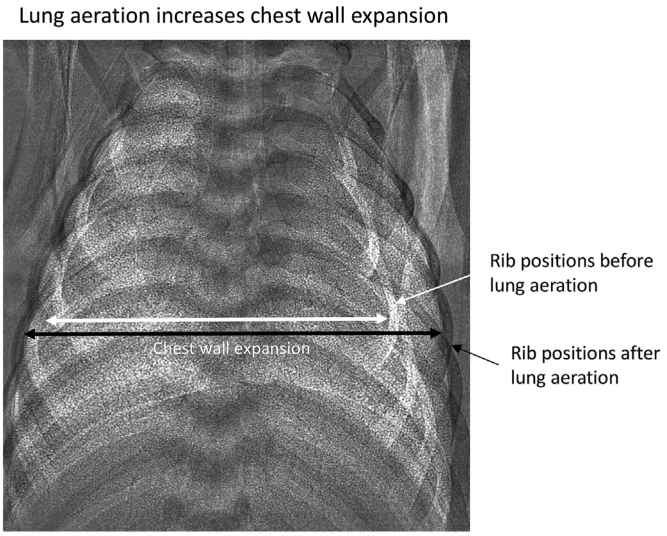
Lung aeration increases chest wall expansion
Rib positions before lung aeration
Chest wall expansion
Rib positions after lung aeration

Fig. 3. Two superimposed phase contract X-ray images acquired from the same newborn rabbit before (inverted image, ribs displayed in white) and following (ribs displayed in black) lung aeration; both images were acquired at functional residual capacity. Note that, based on rib position, the chest wall has considerably expanded following lung aeration.

5. The cardiovascular transition at birth

As described above, the fetal cardiovascular system is considerably more complex than the adult, containing multiple shunts that interconnect the pulmonary and systemic circulations [3] Fig. 4. However, while the fetal and adult circulations are anatomically distinct, functionally they are quite similar, differing only because the placenta, rather than the lung, is the fetal organ of gas exchange. That is, due to the presence of the ductus arteriosus, which shunts blood from the pulmonary artery into the aorta, the right ventricle provides the majority of blood flow to the organ of gas exchange (placenta) in the fetus [3], just like it does in the adult. Similarly, due to the presence of the ductus venosus and foramen ovale, which shunts umbilical venous return directly into the left atrium, blood returning from the gas exchange organ in the fetus, provides the majority of preload for the left ventricle, just like it does in the adult [3,30] Fig. 4. However, as the lungs must take over the role of gas exchange at birth, the circulation has to undergo a massive re-organisation so that the lungs can: (i) become the sole

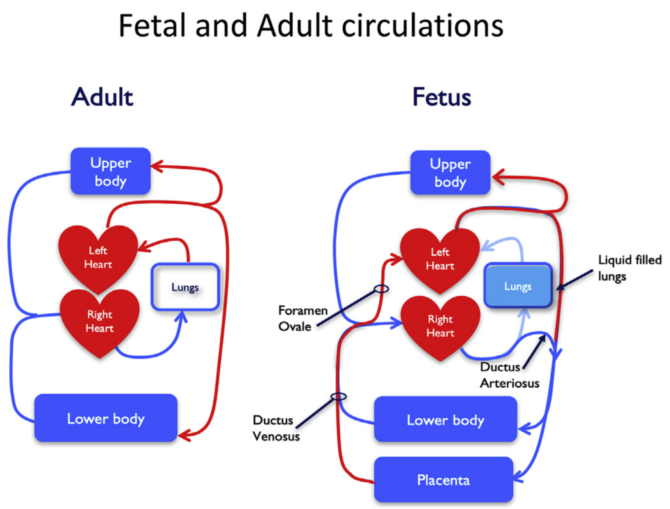

Fig. 4. Functional structure of the adult and fetal circulations. In the adult, all venous return from the upper and lower body returns to the right side of the heart, providing the right ventricle with preload. As all of right ventricular output flows through the lungs, pulmonary venous return provides all preload for the left ventricle. In the fetus, pulmonary blood flow (PBF) is low as the majority of right ventricular output flows through the ductus arteriosus into the descending aorta, with much of this blood flowing through the placenta. As such, PBF provides little preload for the left ventricle, which instead comes from umbilical venous return via the ductus venosus and foramen ovale. While the fetal circulation is anatomically quite distinct from the adult circulation, functionally it is quite similar in that the right ventricle provides all or most of the flow to the organ of gas exchange (lung and placenta). Similarly, the left ventricle receives its preload predominantly from venous blood returning from the organ of gas exchange.

recipient of blood flow exiting the right ventricle and (ii) provide sufficient venous return to sustain left ventricular output. The primary factor that underlies these changes is a very large decrease in pulmonary vascular resistance (PVR), which in turn is triggered by the one event that cannot occur before birth, lung aeration [2].

6. Increase in PBF at birth

Increased vasodilator release, particularly nitric oxide (NO), in response to an increase in oxygenation, is thought to be the primary mechanism that stimulates an increase in PBF in response to lung aeration [31]. Indeed, oxygenation is an important regulator of PBF in adults, being largely responsible for ventilation/perfusion matching in the lung. However, while, increasing oxygen levels can increase fetal PBF, the effect of oxygen is not sustained [31] and ventilation of the lung with a gas devoid of oxygen (ie 100% nitrogen) or with low oxygen levels, can stimulate a large increase in PBF [32,33]. Thus, other mechanisms are also involved, which include, an increase in lung recoil caused by the formation of an air/liquid interface and the creation of surface tension within the lung following aeration [34]. However, while deflating the fetal lung increases PBF, the increase is considerably smaller than the increase in PBF at birth [34].

Recent imaging experiments have discovered a previously unknown mechanism for the increase in PBF at birth while investigating the spatial relationship between lung aeration and the increase in PBF [35–37] Fig. 5. In view of the effects of oxygenation and lung recoil on PBF, it was hypothesized that, at birth, the increase in PBF would be restricted to aerated lung regions [37]. However, partial lung aeration was found to cause a global increase in PBF (Fig. 2), which occurred equally and simultaneously in all parts of the lung, irrespective of their aerated state Fig. 5. Similarly, partial aeration of the lung with a gas devoid of oxygen (100% nitrogen) also caused a global increase in PBF [35]. As such, the global response cannot be due to increased oxygenation following recirculation of oxygenated blood from aerated into unaerated lung regions. On the other hand, as partial lung aeration with 100% oxygen caused a larger PBF increase in aerated regions, compared to unaerated regions [35], increased oxygenation likely contributes to the increase in PBF at birth, but the effect is localised to aerated lung regions.

Realisation that partial lung aeration causes rapid vasodilation simultaneously in aerated and unaerated regions, led to the hypothesis that a neural reflex mediates the lung aeration induced increase in PBF [36]. In the adult lung, the juxta-capillary receptor (J-receptor), is thought to be sensitive to lung oedema and when activated triggers an increase in breathing rate (tachypnoea) [38]. The receptors are thought to be located within juxta-capillary tissue between adjacent alveoli and to signal via afferent C-fibres passing within the vagal nerve trunk. As lung aeration at birth involves lung liquid leaving the distal airways and entering the peri-alveolar tissue, the accumulation of liquid within lung tissue simulates lung oedema and may activate these J-receptors. The receptors signal the brain via the vagus which then initiates global pulmonary vasodilation, presumably via efferent parasympathetic nerves. This hypothesis is consistent with the finding that bilateral *trans*-section of the vagus nerves [36] blocked the global increase in PBF caused by partial lung aeration. Interestingly, partial lung aeration with 100% oxygen increased PBF only in aerated lung regions, indicating that the oxygen mediated increase in PBF was not affected. As such, the increase in PBF at birth in response to lung aeration may result from a hierarchy of mechanisms that either have global or localised effects. That is, the initial movement of liquid out of the airways into lung tissue activates receptors (possibly J-receptors) to initiate a global increase in PBF via a neural reflex. However, this increase in PBF is modulated at the local level by increased oxygenation, which is likely to be mediated by NO release.

7. Why should lung aeration initiate a global increase in PBF?

In the healthy adult lung, ventilation of lung regions is closely “matched” with the level of blood flow (perfusion) through those lung regions, which is known as “ventilation/perfusion matching” [39]. This is largely regulated by changing oxygenation levels within localised lung regions and plays an important role in optimising the lung's gas exchange potential. This is achieved by ensuring that when ventilation within lung regions change, affected regions receive a matching change in blood flow. In the diseased lung, a ventilation/perfusion “mismatch” can occur whereby lung regions with little or no ventilation receive large amounts of blood flow. This is commonly referred to as a pulmonary shunt and can greatly reduce the gas exchange efficiency of the lung.

While a ventilation/perfusion “mismatch” is thought to be problematic in adults, the presence of a large pulmonary shunt in newborns at birth can be viewed in a very different context [37]. Indeed, while survival at birth is not dependent upon the entire lung being ventilated, good cardiac output is essential for preventing hypoxic/ischemic brain injury during periods of reduced oxygenation, which is relatively common at birth. Thus, as a high PBF is essential to maintain left ventricular output, it is important that the increase in PBF is not limited by whether or not the lung is fully aerated. As lung aeration can be delayed in some infants, particularly very preterm infants, it makes good teleological sense that cardiac output is not limited by the degree of lung aeration.

8. Cardiovascular effects of umbilical cord clamping at birth

As discussed above, during fetal life, PBF is low and contributes little to the supply of preload for the left ventricle, which instead primarily comes from umbilical venous return [3,30]. Thus, after birth the supply of preload for the left ventricle must switch from umbilical venous return to pulmonary venous return, but before this can happen,

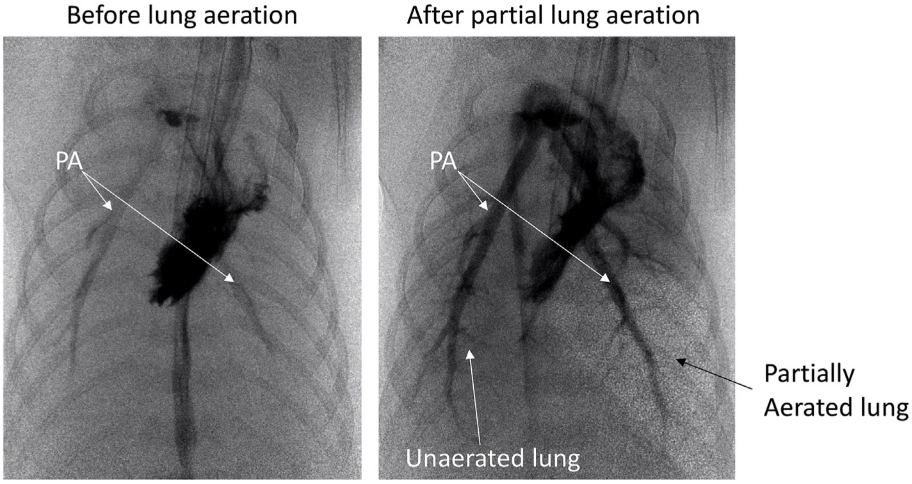

Fig. 5. Simultaneous angiographic and phase contrast X-ray images of a newborn rabbit before and after lung aeration. Very little iodine contrast flows into the pulmonary arteries (PA) before lung aeration, which is indicative of low PBF. Following partial aeration of the lung, PBF markedly increases in both PAs, increasing equally in both arteries irrespective of whether they are perfusing aerated or unaerated regions of the lung.

the lungs must aerate so that PBF can increase [40,41]. As such, when umbilical cord clamping occurs immediately after birth, before the lungs have had an opportunity to aerate, the loss of umbilical venous return causes a loss of preload and a sudden reduction in cardiac output [40]. Cardiac output remains low until the lungs aerate and PBF increases to restore venous return to the left ventricle [40]. In addition, the loss of the low resistance placental circulation upon cord clamping causes a large rapid increase in systemic vascular resistance, resulting in a rapid rise in arterial pressure (30% increase in 4 heart beats) [40]. As a result, umbilical cord clamping before lung aeration not only causes a loss in ventricular preload, but also causes a large increase in after load, which likely contributes to the reduction in cardiac output [40].

The question of whether immediate cord clamping before lung aeration could impact on cardiac output at birth was first raised by the study detailing the nomograms for heart rate changes from birth in normal healthy well oxygenated infants [42]. Up to 50% of normal healthy infants were found to be bradycardic (heart rate < 100) within the first minute of birth, which was difficult to explain simply in terms of a hypoxia-mediated bradycardia [42]. Instead it was suggested that the loss of umbilical venous return due to cord clamping caused a large reduction in cardiac output, which was reflected by a decrease in heart rate [42]. This suggestion was subsequently confirmed in animal studies, which also demonstrated that if lung aeration and the increase in PBF occurs before umbilical cord clamping, the reduction in cardiac output is avoided [40]. This is now referred to as physiological based cord clamping (PBCC) and provides an additional or alternative explanation for the benefits of delayed umbilical cord clamping [2,43,44].

9. Delayed umbilical cord clamping

Until recently, the benefits of delaying or deferring umbilical cord clamping (DCC) immediately after birth has entirely centred around the concept of placental transfusion [45,46]. This is thought to result from a net shift of blood volume out of the placenta into the infant in a time-dependent manner after birth [47]. Compared with immediate cord clamping, the infant body weight gains associated with placental transfusion during DCC [45] are consistent with the reduction in birth weight found in the meta-analysis comparing active vs expectant management of the third stage of labour [48]; immediate cord clamping is one of three components of the active management strategy. As such, the evidence for “placental transfusion” is compelling [49], but as yet there is still no scientific data explaining how this occurs and it is possible that the word “transfusion” is misleading. It is not gravity related [50,51], it is not due to uterine contractions “squeezing” blood out of the placenta (unpublished observations), it is not due to the increase in PBF causing a reduction in umbilical artery flow [52] and it is not due to intrathoracic pressure reductions caused by inspiration [53]. It could result from a shift in blood volume out of the infant and into the placenta during vaginal birth, which then shifts back to to "rebalance" the circulations after delivery. But this needs verification. Nevertheless, the focus on “placental transfusion” has meant that the vast majority of clinical trials on DCC have used a time-based approach, because placental transfusion is thought to be time-dependent [45,46]. However, we now know that a time-based approach makes little biological sense and is less than ideal, particularly for infants requiring respiratory support at birth [2,43]. Indeed, those infants will either receive immediate cord clamping or have their respiratory support delayed so that they can receive a “placental transfusion”. As indicated above and below, the science is very clear and predicts that both strategies are far from ideal, particularly the latter.

10. Physiological based cord clamping (PBCC)

The concept underpinning PBCC is quite simple. That is, at birth, if the lung aerates and PBF increases before the cord is clamped, then PBF is able to immediately take over the role of providing preload for the left ventricle following cord clamping [2,43]. This avoids the reduction in cardiac output caused by the loss of umbilical venous return upon cord clamping [40]. In addition, cord clamping after lung aeration greatly mitigates the increase in arterial pressure caused by cord clamping, because the lung becomes an alternate low resistance pathway for blood flow for both left and right ventricles [40,41]. As a result, left-to-right shunting through the ductus arteriosus increases, leading to a further increase in PBF and venous return to the left ventricle [41]. On the other hand, clamping the umbilical cord immediately after birth causes a reduction in cardiac output that is sustained until after the lungs aerate and PBF increases [40]. As such, if lung aeration is delayed, cardiac output will remain reduced throughout this period. Then, after lung aeration, cardiac output is rapidly restored, causing a rebound in arterial pressure and a large increase in cerebral blood flow [40]. It is not surprising therefore, that one of the noted benefits of DCC is a reduction in IVH [49].

While PBCC can sustain cardiac output immediately after birth and may protect the brain from vascular damage, the logistics of helping infants, particularly very preterm infants, aerate their lungs with an intact umbilical cord was, until recently, thought to be unfeasible. However, recent feasibility studies have demonstrated that the logistical issues are not insurmountable [54]. One study (Baby-directed umbilical cord clamping study; Baby-DUCC), assessed the feasibility of stabilising preterm infants (> 32 weeks) with the cord intact by placing the baby on the mum's legs [55]. They found that stabilising infants, as indicated by regular stable breathing, with the cord intact, prevented the bradycardia evident in normal healthy infants immediately after birth. Another study (ABC) has used a purpose-built resuscitation table (Concord table, Concord Neonatal, the Netherlands) that allows for more extensive resuscitation and monitoring of the infant while the umbilical cord remains intact [54,56]. Recent safety and feasibility studies in very preterm infants (< 30 weeks) have shown that all necessary interventions for cardiopulmonary stabilization can be performed while the infant remains attached to the umbilical cord [57]. They also observed less bradycardia and hypoxia at birth, supporting the concept of a more stable haemodynamic transition. As the average cord clamping time was over 4 min [57], this approach also allows preterm infants to maximally benefit from placental transfusion, while not delaying the onset of resuscitation. A number of trials are now in progress that are focussed on PBCC, rather than a time-based approach, and the sub-group of infants that may benefit is being expanded to include other infants likely to experience a long delay between birth and lung aeration. These include infants with a congenital diaphragmatic hernia [58,59].

10.1. Umbilical cord milking

It has been suggested that the “placental transfusion” associated with DCC can be replicated, over a much shorter time period, simply by milking the umbilical cord [60]. Cord milking involves squeezing the cord between thumb and finger and then “miking” the cord towards the infant, forcing any blood in the cord to move into the infant. This milking procedure can occur once or several times along a segment of cord (up to 20 cm long) [60]. It has been suggested that cord milking may be an alternative to DCC and may benefit infants needing resuscitation at birth, allowing them to get a “transfusion” without the delay [60]. However, this assumes that the only benefit of DCC is placental transfusion, which we know is incorrect [2,43]. Furthermore, recent scientific evidence indicates that cord milking is potentially worse than immediate cord clamping, particularly if it is done several times [52]. That is, consecutive milks result in large fluctuations in blood pressure and cerebral blood flow that are potentially injurious [52], particularly if the infant is hypoxic at birth and has a vasodilated cerebral vascular bed. Furthermore, whether or not milking results in a net “transfusion” of blood into the infant depends on the milking procedure, because retrograde flow can occur out of the infant between milks [52].

Some have argued that umbilical cord milking is safe because numerous trials have not detected any harmful effects in infants [60], in apparent contradiction to what would be predicted based on the scientific evidence [52]. However, a recent trial (PREMOD2) in very preterm infants was stopped early due to an increase in IVH rates in milked infants (22% vs 6%) [61]. This finding may provide a clue as to why it is safe in some infants, but increases the risk of cerebral vascular damage in others. Indeed, the scientific studies on PBCC have shown that the impact of cord clamping on arterial blood pressure is greatly mitigated when cord clamping follows breathing onset and the increase in PBF [40]. As such, if cord milking occurs following breathing onset (and the increase in PBF), it will likely have little impact on arterial blood pressure, whereas if it occurs before breathing onset it should cause large fluctuations in pressure. Until recently, most trials examining the effects of cord milking have occurred in healthy near-term infants, who are likely to have commenced breathing immediately after birth [60]. This would be expected to greatly mitigate the pressure fluctuations caused by milking. In contrast, those infants requiring immediate resuscitation at birth were mostly excluded from these trials and, therefore, did not receive milking. However, as very preterm infants have difficulty in aerating their lungs at birth, most will not have aerated their lungs before cord milking. As such, these infants are at high risk of being exposed to the large arterial pressure surges associated with cord milking [52]. Nevertheless, until the science has been thoroughly investigated, it seems prudent to avoid cord milking, particularly in infants requiring resuscitation at birth.

11. Conclusion

In recent years we have learnt much about the cardiorespiratory changes that occur at birth and, in particular, the role of lung aeration in driving these changes. This reinforces the neonatologist's mantra that lung aeration is the key to neonatal resuscitation at birth. While airway liquid clearance can commence during labour, the liquid remaining in the airways after birth and following the first breath is cleared into lung tissue due to the transpulmonary pressures created during inspiration. While this allows the onset of gas exchange, the presence of this liquid in lung tissue can have consequences for respiratory function after birth. In particular, if large volumes of liquid must be cleared into lung tissue, respiratory function can be compromised. This likely explains much of the respiratory distress that can occur in near term infants, particularly TTN. Indeed, as infants born by elective CS without labour will lose little liquid from the nose and mouth, which may explain why these infants are at higher risk of TTN.

Lung aeration also triggers the increase in PBF at birth which is not only important for increasing the efficiency of pulmonary gas exchange, but is also important for providing preload for the left ventricle. During fetal life, preload for the left ventricle is primarily derived from the umbilical vein, but this is lost upon clamping of the umbilical cord at birth. To avoid this, it is logical to aerate the lung and increase PBF before the cord is clamped to avoid the loss in preload and the associated reduction in cardiac output. This is known as PBCC and cannot be replicated by manoeuvres such as cord milking.

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Anticipation and preparation for delivery room emergencies

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ABSTRACT

Effective communication is the keystone in the management of delivery room emergencies. A clearly defined framework and “shared mental model” optimize team collaboration and are essential when anticipating and preparing for high-stakes emergent cases. This review defines a framework to build shared mental models using dialogue, pre-briefing, checklists, simulation, debriefing and structured feedback to maintain a cohesive high functioning team. Strategies to approach different emergency lead-times will be discussed, and case examples will be used to illustrate concepts outlined.

1. Introduction

Delivery room (DR) emergencies are among the highest stakes clinical scenarios a provider may face related to the care of the newborn. Often fraught with wide variability, these emergencies may be anticipated, as a result of a known fetal anomaly within an identified “high-risk pregnancy,” or may only become apparent during labor or resuscitation. Neonatal resuscitation teams should be trained in management of these expected and unexpected DR emergencies.

Anticipation and preparation are central to mitigating uncertainty. In many cases, teams can anticipate risk factors for increased likelihood of more interventions in the DR [1]. The foundation of anticipation and preparation for DR emergencies is built on identifying and gathering optimal information, personnel, and equipment for the resuscitation, while maintaining a shared mental model through effective communication. A recent review by Sawyer et al. outlined methods of anticipation and preparation for every DR resuscitation [2].

The purpose of this report is to build upon those concepts, focusing on how teams can create a shared mental model during DR emergency resuscitation through preparation, debriefing, review, and simulation. Specific medical management of each emergency is beyond the scope of this review.

The discussion will be organized by the time allowed for preparation prior to delivery (see Fig. 1), covering preparation of:

1. Unanticipated emergencies with minimal time to prepare
2. Unanticipated emergencies with no time to prepare
3. Anticipated potential DR emergencies with time to prepare

To consolidate concepts, an institutional example of an antenatally identified case of cloacal malformation complicated by hydrometrocolpos and development of a large intraabdominal collection with resultant pulmonary hypoplasia will illustrate an anticipated potential DR emergency and how multi-disciplinary preparation affected DR management.

2. Shared mental models

The key to successful team management of DR emergencies is effective communication and teamwork [3,4]. Teams can communicate and function more effectively when they have a shared mental model [5,6]. This is defined as “the perception of, understanding of, or knowledge about a situation or process that is shared among team members through communication” and has many benefits for team dynamics.

“Shared mental models can help teams by [7]:

- Leading to mutual understanding of situations
- Leading to more effective communication
- Enabling team members to back up and fill in for each other
- Enable better prediction and anticipation of team needs
- Create commonality of effort and purpose”

In neonatal resuscitation, critical time points for establishing and re-establishing shared mental models are:

- Prior to delivery (with a pre-brief)
- During resuscitation or emergencies (with recaps)
- When reviewing the resuscitation as part of the transition to post-DR care (during the debrief)

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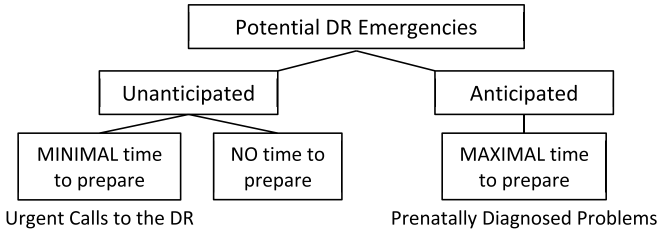

Fig. 1. Anticipation and preparation for delivery room (DR) emergencies.

Table 1
Anticipating and preparing for delivery room emergencies.

For EVERY Individual Delivery	Developing and Maintaining Expertise Globally
Communication with OB	Regular resuscitation review
Communication with the family	Simulation
Equipment/personnel checklists	
Pre-briefing	
Debriefing	

Maintaining a shared mental model from the preparation period before through the stabilization period after resuscitation keeps teams cohesive and helps them respond more expediently to any emergencies that may arise [8].

Table 1 illustrates how shared mental models are established for individual deliveries and how the skills related to them may be practiced and improved on a broader scope. Each element will be discussed in detail.

3. Anticipation and preparation prior to every delivery

3.1. Communication with the obstetric team prior to delivery

Communication with the obstetric team should begin as early as possible. Scheduled times to jointly “run the labor board” may be helpful to provide an overview of imminent deliveries and keep neonatal teams updated on higher-risk deliveries and anticipated admissions to the neonatal intensive care unit (NICU). Prior to each delivery, the “four pre-birth questions” should be ascertained as recommended by the Neonatal Resuscitation Program (NRP). These include gestational age, number of babies, presence of meconium and presence of any additional risk factors [9]. Additional information, such as the review of the fetal heart rate tracing and estimated fetal weight, particularly in the case of preterm infants, may be helpful for framing expectations, choosing equipment (appropriately sized laryngoscope or endotracheal tube) and calculating medication doses prior to delivery.

When called for deliveries, transmission of this information to the responding neonatal provider/team in real time is ideal. This allows early anticipation and preparation, an opportunity for clarification of information and confirms that a neonatal provider/team are aware and will be in attendance of the delivery. Importantly, this also allows for more effective triage of personnel and reallocation of resources, as neonatal providers/resuscitation teams are often pulled from other duties in the newborn nursery or NICU.

3.2. Communication with the family prior to delivery

When possible, introduction of the neonatal team to the family should occur prior to delivery. In high-risk pregnancies, antenatal counseling for sharing information and ascertaining a family's values and preferences is critical to framing neonatal management, particularly when outcomes are uncertain. This should be performed jointly with the obstetrics team prior to delivery when possible [10]. Discussion related to best practice of antenatal counseling is outside the scope of this review.

Table 2
Information to provide families in the delivery room when emergencies are anticipated.

General Preparation	Where will resuscitation occur (if not in the same room as delivery)? What might resuscitation include? When can they expect an update? When will they be able to see the baby?
Specific Preparation	What can they expect the baby to look like? What is a potential timeline for transfer to the NICU? What studies/interventions may occur after birth? Who will evaluate the baby in the NICU (teams/specific providers)? When should the parents expect to be able to speak to someone?

If DR emergencies are anticipated, discussion of where resuscitation occurs (if not in same room as delivery), potential interventions, and providing an estimate of when they will be able to see their baby can be helpful to prepare family expectations and should be prioritized where possible. More detailed preparation and review of postnatal care and expectations should occur when admission to the neonatal intensive care unit (NICU) is anticipated. Table 2 outlines points to consider discussing with families when DR emergencies are anticipated.

3.3. Personnel

Members of the neonatal resuscitation team should be trained in DR management of the newborn and competent in identifying and addressing problems and emergencies if they arise. Inclusion of specific advanced providers or additional personnel can be considered depending on the circumstances and degree of concern identified [11]. If not initially present, methods of reaching these providers, should also be clearly stated. Team members with specific knowledge of the resuscitation area, including where to obtain additional supplies and equipment may be an invaluable resource. Roles of all team members should be clearly delineated prior to delivery, particularly the identification of a team leader [9,12].

3.4. Equipment

Availability of all equipment for neonatal resuscitation is essential for successful resuscitations. This is increasingly true when emergencies arise in the DR. Checklists, such as the NRP “Quick Equipment Checklist” are useful in ensuring all equipment is visually identified and checked prior to delivery [11]. Delegating responsibility so that team members are responsible for checking the equipment necessary in their specific role may streamline the process, particularly when time is limited.

When risk factors identify the need for specific equipment, this should be intentionally stated, especially if that equipment is less commonly used in the DR. These may include equipment for thermoregulation (thermal mattress, plastic bag/wrap) when preparing for the delivery of a preterm infant, or a meconium aspirator when meconium stained amniotic fluid is present.

3.5. The pre-delivery briefing, or “pre-brief”

Pre-briefing is an important method of preparing teams and should be performed prior to EVERY delivery. It allows the team to establish a shared mental model specific to the case, anticipate and prepare for what may occur, and provides an opportunity for team members to raise questions and clarify plans and has been shown to improve teamwork and communication [13].

The pre-brief should include a discussion of the specific risk factors identified, potential interventions the newborn may require, and importantly when and how these interventions integrate into the NRP

Table 3
Elements of the pre-brief.

- Review of specific risk factors identified and problems that may result
  - Discussion of potential interventions that may be required
  - When these interventions will occur in resuscitation/How they integrate into the NRP algorithm
  - Assignment of roles/responsibilities
  - Who/how to call for additional support if needed
  - Equipment Check
  - Review of teamwork principles

algorithm, as well as roles assigned to each member of the team (see Table 3). Contingency plans should be discussed, which may include methods of escalation if additional personnel or equipment are required. A brief reminder of optimal teamwork principles, such as speaking up if concerns are identified, use of closed loop communication, and cross-monitoring, should also be provided [14].

Thorough team pre-briefs are especially critical in large institutions with providers of varying training and experience, and where members of the neonatal resuscitation team are often changing, with new combinations of team members being formed each shift [15]. Establishing this shared mental model and identifying contingency plans result in more organized resuscitations, quicker time to life-saving interventions and improved team functioning [16].

3.6. *Debriefing*

Debriefing is a “facilitated or guided reflection in the cycle of experiential learning” [17].

It serves as a valuable team-reflection exercise to determine the efficacy and accuracy of the anticipation/preparation prior to delivery, assess communication and team dynamics, and review medical decisions made during the resuscitation. Regular group- and self-reflection, leads to changes in ways we conceptualize information and serves as the next step in the cycle of learning [18]. This reflective process helps individuals and teams continuously improve their abilities to anticipate, prepare and communicate in emergency scenarios and informs future performance.

Debriefing should occur after every delivery, and especially after critical events. It may be brief and take the form of “plus-delta,” where teams review things that went well and things that could be improved upon [19]. Debriefing tools or scripts are helpful in guiding facilitators and teams through the process and serve as a platform for starting these discussions [2,20].

4. Developing and maintaining expertise in management of DR emergencies

Beyond individual deliveries, anticipation and preparation for DR emergencies should occur on an institutional level. This may occur through regular review of resuscitations to identify areas for ongoing improvement, or development and maintenance of expertise through simulation.

4.1. *Review of resuscitations*

Regular review of collected debriefings from individual resuscitations, particularly where DR emergencies were present, provides neonatal resuscitation programs a forum to ensure ongoing quality improvement on a broader scale [21,22]. Multi-disciplinary representation is optimal for productive discussions in this forum and may include neonatal and obstetric physicians, nurse practitioners, nurses, trainees (fellows/residents), respiratory therapists, educators and potentially others.

Through the lens of these diverse perspectives, problems identified in debriefings, such as those related to equipment, systems or processes, may be further defined and addressed and joint solutions arrived at more quickly. Broad knowledge gaps may be identified and methods of integrating these topics into educational curriculum discussed. Review of details of individual cases may also aid in large-group reflection on practice [8].

This forum also serves as a point of communication between two closely tied clinical services. Regular discussion keeps all team members abreast of changes in staff, equipment, policy, procedures, etc. on either unit, while providing an opportunity for feedback.

4.2. *Use of simulation to develop expertise in the management of DR emergencies*

4.2.1. *General preparation*

Resuscitation reviews can be coordinated with simulation programs to further characterize problems, streamline processes and build clinical expertise in scenarios of DR emergencies. These emergencies may arise in various forms (a “difficult airway”, hypovolemia, etc.), in various areas and with varying amounts of warning. Simulation provides a low-stakes setting to practice and prepare for all of these high-stakes scenarios.

When designing these multi-disciplinary simulations, learning objectives will center around the rapid identification and management of clinical emergencies. In addition to focusing on knowledge and clinical skills, training sessions should also include review of hospital policies and procedures. As examples, in the case of the “difficult airway,” escalation protocols and methods of contacting sub-specialty support during an active resuscitation should be regularly reviewed and tested. In the case of profound hypovolemia, training may include review of procedures to emergently access and deliver un-crossmatched, O-negative blood.

Difficulty of scenarios may be titrated commensurate with the experience of the team. For example, for more experienced teams, limited information may be provided in order to challenge team members to ask specific information that will be helpful for the resuscitation, and the time allowed for anticipation and preparation prior to “delivery” may be decreased. Conversely, difficulty may be titrated downwards for less experienced teams by providing more information and time prior to the start of the scenario. When debriefing these scenarios, specific focus should be placed on how anticipation and team preparation prior to delivery facilitated resuscitation, and how to perform these critical steps more expeditiously.

Simulation scenarios may also be written to mirror upcoming high-risk deliveries (such as the scheduled delivery of an infant with a neural tube defect). This offers teams a “dress rehearsal” and additional opportunity of anticipating and preparing for situations that may arise in the delivery room.

In situ simulations in all clinical areas that emergency resuscitations may occur will also benefit team preparation [23]. Performing simulations in active clinical areas (e.g. operating rooms or DRs) offers increased realism, providing an opportunity for team members to familiarize themselves with the setting and particular challenges of the space [24]. In situ simulations may also identify problems related to staffing, communication and equipment, and provide a method of testing potential solutions, without bringing harm to a patient [23]. This may be especially helpful in settings where neonatal resuscitation occurs infrequently and delays to getting appropriate equipment or lack of familiarity with the clinical area may lead to delays in appropriate intervention, resulting in progression from a less severe problem to an emergency. These settings may include the emergency room, triage area of the labor and delivery unit and the antepartum area. Information uncovered during these simulations should be disseminated and reviewed with members of the resuscitation team.

4.2.2. *Use of simulation to prepare for specific, anticipated DR emergencies*

In addition to the preparation for general DR emergencies, simulation may also be utilized in high-risk deliveries, where fetal anomalies have been identified and specific DR emergencies may be anticipated. In these scenarios, simulation can be employed to develop, test and optimize resuscitation plans and serve as a "dress rehearsal" for practice.

Patient specific models or manikins can be built to provide team members with a realistic replica of the anomalies and challenges they may face in the DR [25,26]. Using this model, the multi-disciplinary and sub-specialty teams involved in the delivery can trial different approaches and strategies to resuscitation and identify an optimal method. After the plan is established, the team can practice the orchestration of a complex resuscitation as well as anticipated emergencies that may arise [27].

Given the large numbers of people at times required at these deliveries, in-situ simulation may also help to further refine the resuscitation plan. Simulation in the actual DR setting will provide a more accurate sense of space allotted to each person, lighting, noise and identify other ergonomic issues [24]. These in turn will inform ideal placement of personnel and equipment. This may be especially useful for those who are unfamiliar with the DR and its typical set up.

5. Potential emergencies arising just prior to delivery – MINUTES to anticipate and prepare

Emergencies arising just prior to delivery often result in urgent calls to the DR, where time for team preparation is limited (see Fig. 1). Examples of these may include preterm birth (< 28 weeks), maternal trauma, umbilical cord prolapse, significant fetal heart rate abnormalities and presence of thick meconium. These cases represent high-risk deliveries with an increased likelihood that the newborn will not respond to the initial steps and bag mask ventilation [1]. Teams should anticipate that these newborns may require advanced maneuvers such as placement of an advanced airway, chest compressions, medications or additional interventions not usually employed in routine resuscitation.

For each risk factor identified, resuscitation teams should anticipate related problems or emergencies that may occur, along with potential interventions. All of these should be clearly discussed in the pre-brief so that the neonatal team forms a shared mental model of the anticipated resuscitation. Table 4 provides examples of risk factors and their potential problems and related interventions.

As an example, in the case of a preterm infant (< 28 weeks), specific DR challenges relate to lung immaturity and respiratory distress syndrome (RDS), difficulty establishing a functional residual capacity (FRC) and high risk of heat loss. To address the first risk factor of lung immaturity, potential interventions may include immediate use of positive end expiratory pressure (PEEP) for lung recruitment and alveolar stabilization, starting at a higher fraction of inspired oxygen (FiO_2) (30% vs 21%), and need to escalate to higher peak inspiratory pressures (PIP) initially. For the risk of heat loss, use of a thermal mattress and plastic bag/wrap immediately after birth, with placement of a temperature probe to ensure thermoregulation may be performed. Additionally, given that preterm infants may decompensate very quickly when poorly ventilated, early placement of an electrocardiogram (ECG) can direct resuscitation and provide expedient feedback on effectiveness of interventions. And given the preterm infant's vulnerability to oxygen exposure, early placement of a pulse oximeter will aid in targeting oxygen delivery. Promptly addressing ventilation in the context of presumed RDS and risk of heat loss during the resuscitation of this preterm newborn will hopefully prevent emergencies from arising (such as prolonged poor ventilation leading to the need for chest compressions) [28].

6. Unexpected emergencies arising at/after birth – NO TIME to anticipate and prepare

Unanticipated emergencies may arise during the birth process or resuscitation itself, requiring teams to identify and address problems in real time (see Fig. 1). These should be considered if the depressed neonate fails to respond as expected to routine resuscitation and provision of effective ventilation. Examples may include potential exposure to intrapartum hypoxia-ischemia, hypovolemia secondary to an acute fetomaternal hemorrhage, undiagnosed airway malformation or pneumothorax (see Table 5).

Effective team management during an emergency should focus on clear communication and use of "recaps" as necessary to establish/re-establish a shared mental model [29]. In situations where an unanticipated emergency arises, it is not uncommon for team members to break off into silos to gather more information and troubleshoot reasons for failure of the newborn to respond to expected interventions. This often results in increasing noise and lack of consensus, leading to loss of critical information and increasing stress among the team and onlookers (which may include parents).

6.1. Use of recaps

The use of "recaps" is helpful to quiet the room and re-organize the team. Stated by a single person, often the team leader [29], recaps include a brief description of what is known and unknown, current

Table 4
Examples of anticipating potential problems and interventions based on risk factors identified prior to delivery.

Risk Factors	Potential problems	Potential Interventions
Preterm birth (< 28 weeks)	RDS Difficulty establishing FRC Risk of heat loss	Use of PEEP, may require higher PIP to start Consider starting at 30% FiO_2 Early placement of monitoring devices Use of thermal mattress and plastic bag/wrap
Placental abruption	Potential for hypoxia-ischemia Respiratory depression	Intubation, UVC, chest compressions ± epinephrine
Maternal trauma	Hypovolemia Hypoxia-Ischemia Birth injuries	Volume (O-neg blood or normal saline) UVC, chest compressions ± epinephrine Careful handling and complete survey
Umbilical cord prolapse	Potential for hypoxia-ischemia Hypovolemia	UVC, chest compressions ± epinephrine Volume (normal saline)
Potential shoulder dystocia	Birth injuries	Careful handling and complete survey
Significant fetal heart rate abnormalities	Potential for hypoxia-ischemia Respiratory Depression	Intubation, UVC, chest compressions ± epinephrine
Presence of thick meconium	Tracheal obstruction MAS	Use of meconium aspirator for airway clearance Needle thoracentesis if pneumothorax present Use of higher PIP

RDS: respiratory distress syndrome, FRC: functional residual capacity, PEEP: positive end expiratory pressure, PIP: peak inspiratory pressure, FiO_2: fraction of inspired oxygen, UVC: umbilical venous catheter, MAS: meconium aspiration syndrome.

Table 5
Unexpected emergencies arising in the delivery room.

Perinatal depression secondary to hypoxia ischemia
Hypovolemia
Difficult airway
Undiagnosed airway malformation
Pneumothorax
Emergencies related to birth injuries
Undiagnosed critical congenital heart disease

problems and review of the timeline and interventions that have occurred. This serves as a platform for team members to share critical information and brainstorm as a group to identify potential solutions if resuscitation is not proceeding as anticipated. Recaps serve as brief "time-outs" in the middle of a resuscitation and may help function as a "reset," forcing team members to step outside of their individual concerns and break down silos that may have naturally formed. While this pause may be viewed as loss of critical time during an emergency, recaps are invaluable in sharing information and re-establishing a shared mental model, which re-focuses and re-prioritizes the group to a common goal.

7. Expected emergencies (known fetal anomalies and/or characterizization as a "high-risk" pregnancy) – WEEKS/MONTHS to anticipate and prepare

Through partnerships with obstetrics and maternal-fetal medicine (MFM), neonatal teams are often alerted to the complex, high-risk fetus during pregnancy (see Fig. 1). This allows time to gather clinical information about the anomalies present, follow the growth and development of the fetus, determine the potential impact of anomalies on mortality and short-/long-term morbidities, and have detailed discussions with the families about their values and preferences. After this information is gathered, multidisciplinary teams work together to anticipate and prepare for the high-risk delivery, detailing algorithms for prioritizing interventions based on the clinical scenarios present at birth.

7.1. Gathering information

Improvement in pre-natal imaging and diagnosis allows unprecedented insight into fetal anomalies. In addition to ultrasonography (US), magnetic resonance imaging (MRI) and fetal echocardiography (echo), are additional modalities more commonly utilized to gain greater anatomic and physiologic information about the fetus. This allows obstetric, neonatal and subspecialty teams to better anticipate the potential interventions that may be required and customize approaches to resuscitation.

7.2. Fetal care teams – coordinating information and streamlining care

If DR emergencies are anticipated, transfer of care and delivery at a hospital with high-risk MFM providers, advanced neonatal providers and subspecialty availability is recommended [30–32]. Inclusion of pediatric sub-specialists in the discussion of potential impact on the fetus can provide a holistic view of interventions required, risk of mortality, lifetime morbidities, and potential impact on the family [33].

Given the complexity involved in defining and predicting outcomes in fetal anomalies and the need for multidisciplinary involvement in counseling, planning and management, centers are increasingly establishing fetal care teams to coordinate management of high-risk fetuses and pregnancies [34,35]. Regular, multi-disciplinary discussion of cases maintains shared mental models among large teams with regard to understanding all the problems related to the developing fetus and facilitates prioritizing management [36].

This coordination of care is particularly important for families of fetuses which may have several complex anomalies. In this case, having each subspecialist understand how their "problem" fits into the larger picture, can help limit confusion during counseling, ensuring that the message to the family remains the same from provider to provider. Importantly, this multi-disciplinary support links the continuum of care, allowing smooth transitions from pregnancy, to delivery, through neonatal care and into childhood.

In addition to the obstetrics/MFM, neonatal and sub-specialty providers, ancillary staff are also integral to the overall care of the family and fetus with complex anomalies. These may include social work, child life (to help families frame transmission of information to other children), and palliative care teams. Finally, a central coordinator within the team may serve as a point of contact with families, helping to streamline care, direct questions and dispel further confusion [37].

7.3. Integrating the family into medical decision making and planning with a known, potentially lethal anomaly

As information is gathered and potential interventions and outcomes are anticipated, in depth discussion with the family should also occur. Gathering as many of the sub-specialty teams to meet simultaneously with the family as possible can be helpful to provide a holistic view of management options. Moving beyond just survival, this can provide the family with a more complete perspective on the necessary short- and long-term interventions and help them make personal judgements on the impact these may have on quality of life. This may be critical in helping families come to decisions on goals of care and decisions related to management of the pregnancy and any emergencies that may arise in the DR. Social work and palliative care providers may also be helpful resources.

7.4. Developing a DR resuscitation plan – anticipating potential emergencies

Once information about the fetus/pregnancy have been gathered, the appropriate multi-disciplinary team has been assembled, and the parents have expressed their values and preferences for resuscitation of the newborn, preparing a detailed DR resuscitation plan may begin.

As previously described, this planning should begin with anticipation of all potential problems and emergencies that may arise due to the anomalies described in the fetus. From here, specific equipment should be listed and potential interventions and management strategies in the DR discussed.

Table 6 provides a summary of critical information to gather for planning, specific equipment and potential DR strategies as they related to a sampling of categories of fetal anomalies [38,39]. This is by no means exhaustive and readers should refer to other articles for details of specific management in the DR for particular anomalies of interest.

Once the team has anticipated potential emergencies that may arise, potential DR strategies and a detailed resuscitation plan should be established. Additionally, contingency plans and activation protocols should be reviewed. This information should next be tested and refined in simulation. Once finalized, it can be shared with the larger resuscitation team and reviewed again prior to delivery.

8. Case study: cloacal dysgenesis with uterine duplication anomaly and hydrometrocolpos

A 28-year-old G1P0 woman was referred to our institution for evaluation of a large cystic structure in the abdomen/pelvis identified on fetal ultrasound at 25 weeks gestational age.

Imaging of lesion:

- 27 weeks: Ultrasound performed demonstrated moderate urinary ascites and a midline bi-lobed cystic structure superior to the bladder.

Table 6

Examples of considerations when preparing a delivery room resuscitation plan where emergencies may be anticipated.

Categories of Fetal Anomalies	Critical Information to Gather for Planning	Specific Equipment[a]	Potential DR Strategies
Obstructive Airway Malformations Pierre Robin Cervical teratoma CHAOS	● Upper airway anatomy ● Presence of other anomalies ● Presence of polyhydramnios ● Presence of hydrops	● Specialized equipment required by advanced airway team[b] ● Supplies for centesis[c] ● Equipment for placement of tracheostomy	● Number/timeframe of attempts at intubation prior to tracheostomy ● When to consider centesis if hydrops present
Congenital Cardiac Disorders Pulmonary atresia TGA Hypoplastic left heart	● Anticipated post-natal need for PGE	● Access – emergency UVC ● PGE ● Normal saline ● ECG	● When to consider PGE ● When to consider volume to improve systemic perfusion
Thoracic Disorders CDH CPAM BPS	● Risk/severity of pulmonary hypoplasia ● Presence of other anomalies ● Presence of hydrops	● Orogastric tube (OGT) ● Access – emergency UVC ● Supplies for centesis ● EXIT/ECMO team and equipment readiness	● Ventilation strategy based on thoracic disorder ● When to place OGT for abdominal decompression ● Ventilation/oxygenation strategies for degree of pulmonary hypoplasia anticipated[d] ● When to perform needle thoracentesis ● When to consider centesis if hydrops present
Abdominal Wall Defects Gastroschisis Omphalocele	● Size of omphalocele[e] ● Extra-abdominal viscera	● OGT ● Sterile bag, plastic wrap	● Immediate OGT for abdominal decompression ● Consideration of early intubation ● Preferred methods of dressing defect in DR to prevent insensible fluid losses/injury to viscera
Skeletal Dysplasia Osteogenesis imperfecta Achondroplasia	● Upper airway anatomy ● Risk of pulmonary hypoplasia ● Presence of other anomalies	● Supplies for thoracentesis	● Ventilation/oxygenation strategies if pulmonary hypoplasia present When to perform needle thoracentesis ● High risk for fracture
Genitourinary Anomalies Bladder exstrophy Cloacal exstrophy	● Presence of other anomalies	● Sterile bag, plastic wrap, dressing ● Umbilical tape •OGT	● Preferred methods of dressing defect in DR to prevent insensible fluid losses, injury to viscera or exposure to infection ● Replacement of clamp with umbilical tape to prevent injury to bladder
LUTO PUV Urethral atresia	● Onset of oligohydramnios risk/ severity of pulmonary hypoplasia	● Supplies for thoracentesis	● Ventilation/oxygenation strategies if pulmonary hypoplasia present ● When to perform needle thoracentesis
Hydrops Fetalis	● Determine underlying cause (treat/ correct if possible) ● Assess risk/severity of pulmonary hypoplasia	● Supplies for centesis	● May require thoracentesis, paracentesis and/or pericardiocentesis ● Ventilation/oxygenation strategies if pulmonary hypoplasia present ● Establish central access early
Sacrococcygeal Teratomas	● Cardiac function (risk of high output cardiac failure) ● Presence of hydrops	● Emergency UVC ● O-neg blood or volume available ● Supplies for centesis	● Risk of membrane rupture and blood loss ● When to consider centesis if hydrops present and affecting ventilation
Neuromuscular Disorders X-linked myotubular myopathy CMD	● Presence of polyhydramnios and risk for pulmonary hypoplasia ● Presence of contractures	● Supplies for thoracentesis	● Ventilation/oxygenation strategies if pulmonary hypoplasia present ● When to perform needle thoracentesis

CHAOS: congenital high airway obstruction, TGA: Transposition of the great arteries, PGE: prostaglandin E, CDH: congenital diaphragmatic hernia, BPS: bronchopulmonary sequestration, LUTO: lower urinary tract obstructions, PUV: posterior urethral valves, CMD: congenital myotonic dystrophy.

[a] Special equipment in addition to standard equipment that should be present at every delivery.

[b] "Advanced airway team" may be pediatric otorhinolaryngology (ENT) and/or anesthesia. Choice of one or both dependent on local practice.

[c] May include pericardiocentesis, thoracentesis or paracentesis depending on presence of hydrops and space involved.

[d] Ventilation/oxygenation strategies in pulmonary hypoplasia may include: use of higher PIP and FiO_2 and use of PEEP. Teams should be aware that newborns with pulmonary hypoplasia are at high risk for developing air leaks and may require needle thoracentesis if there is impairment in ventilation

[e] Giant omphaloceles are associated with respiratory distress and pulmonary hypoplasia.

- 28 weeks: Fetal MRI demonstrated a bilobed cystic structure within the pelvis representing uterine anomaly with associated hydrometrocolpos, bilateral pyelectasis, and moderate abdominopelvic ascites. Lung volumes were diminished, and the amniotic fluid volume was normal to decreased.

Other studies:

- Fetal echocardiogram: single umbilical artery, absent ductus venosus and pericardial effusion (resolved by 31 weeks gestation).
- Amniocentesis: declined.

Social:

- 32 weeks: Family met with Fetal Care Team including MFM, neonatology, pediatric urology and pediatric surgery teams to discuss findings and suspected diagnosis of cloacal dysgenesis with uterine duplication anomaly. Additional findings of pulmonary hypoplasia (and subsequent complications), DR and neonatal interventions were described, as well as severity of potential short-/long-term morbidities.

A follow up MRI performed at 34 weeks gestational age demonstrated that the hydrometrocolpos had increased in size, with severely decreased amniotic fluid volume and severely hypoplastic lungs. The plan was for delivery at 35 4/7 weeks after a betamethasone course.

DR preparation began at 34 weeks gestational age.

- Anticipated problems/emergencies: Given large hydrometrocolpos and worsening compression of lung fields, there was a strong suspicion for pulmonary hypoplasia. If ventilation was poor and heart rate remained low despite intubation, it could be related to upward compression on the diaphragm/lungs or development of pneumothorax. Estimated fetal weight established.

- Equipment required: In addition to standard NRP equipment, other supplies included those for umbilical catheterization and peripheral IV access, thoracentesis (including transilluminator), and placement of a pigtail catheter. Inhaled nitric oxide and high frequency oscillatory ventilator were on standby in the NICU
- Personnel required at the delivery and roles/potential roles included:
  - Neonatal attending ×2 – first as team leader, second available for procedures
  - Neonatal fellow – perform immediate intubation, potential needle thoracentesis
  - Neonatal nurse practitioner – auscultation of heart rate, UVC placement, potential needle thoracentesis
  - Pediatric urology attending and resident – paracentesis for abdominal decompression
  - Pediatric radiology attending – provide ultrasound guidance for pigtail placement
  - Pediatric surgery attending and resident – on standby, backup for paracentesis
  - Neonatal nurse 1 – place ECG and pulse oximeter, first to provide chest compressions if required
  - Neonatal nurse 2 – draw up medications if needed
  - L&D nurse 1 – runner for supplies, liaison for parental updates
  - Pediatric resident – recorder
  - Respiratory therapy – prepare airway supplies, secure airway, take over bag mask ventilation
- Multiple simulations were performed to identify ideal positioning of team members and placement of equipment for interventions in the DR.
- The resuscitation plan included:
  - Initial steps
  - Placement of pulse oximeter on right hand
  - Immediate intubation with 3.5 endotracheal tube
  - Due to pulmonary hypoplasia, use of increased PIPs and higher FiO_2 were anticipated. Team should start at PIP of 25 cmH_2O and increase as needed to "move" the chest. In addition, FiO_2 should be titrated according to pre-ductal saturation targets with the expectation that the infant would likely require rapid escalation in oxygen to 100% initially and gradual titration down with stabilization
  - If heart rate did not improve despite intubation and positive pressure ventilation:
    - Drainage of the hydrometrocolpos would be prioritized if there was adequate chest rise and bilateral air entry was appreciated. In this instance urology would place a pigtail catheter under ultrasound guidance with radiology assistance, and drain the collection until effective ventilation could be achieved
    - Needle thoracentesis would be prioritized if there was poor chest rise and aeration (particularly if unilateral), and the abdomen was soft. Transillumination could be attempted to verify presence of pneumothorax if time allows
  - Needle thoracentesis would be performed if there was persistent hypoxemia with normal/improving heart rate
  - If paracentesis and needle thoracentesis did not result in improvement in heart rate, parents would be informed, and comfort care again offered.

At 35 weeks gestation, the neonatal team met again with the family to review the case and discuss the MRI findings of enlarging uterine mass and significant pulmonary hypoplasia. The parents were counseled that the baby would be intubated immediately after delivery with the possibility of needle thoracentesis and pigtail catheter placement for abdominal decompression if either was thought to be impeding ability to effectively ventilate. After stabilization, the baby would be brought to her side and then quickly taken to the NICU for further management.

8.1. DR course

A female infant was delivered via planned primary cesarean section at 35 4/7 weeks gestation. On brief examination, the infant appeared limp and apneic. There were no grossly dysmorphic facial features or abdominal wall defects. There was a normal labia majora, labia minora, and clitoris with a single perineal opening. Anal atresia was noted.

The newborn was intubated by two minutes of life with initial increase in heart rate from 20s to 70s. Oxygen saturations were in the 30s on 100% FiO_2. The heart rate did not subsequently increase despite appreciable chest rise and bilateral aeration on auscultation. An eight French percutaneous pigtail catheter was placed by urology under ultrasound guidance in the left hemi-abdomen (into the uterus) by six minutes of life, with removal of 150 mL of yellow fluid consistent with urine. Subsequently, the heart rate increased to > 100 beats per minute (bpm) by 13 min of life, without improvement in saturations. Needle thoracentesis was performed on the left chest for persistent hypoxemia and decreased breath sounds, with 44 mL of air removed. Saturations subsequently increased to the mid-80s. Apgar scores were 1/1/3/7 at 1/

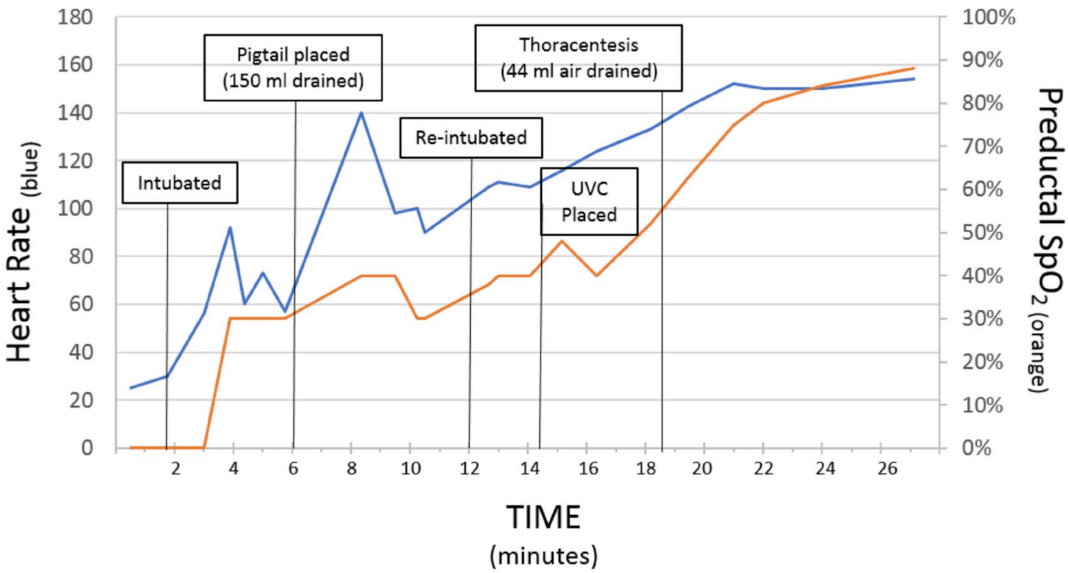

Fig. 2. Heart rate and oxygen saturations with interventions performed during delivery room resuscitation.

5/10/15 min respectively. The newborn was transferred to the NICU at 27 min of life. No chest compressions were performed. Fig. 2 depicts heart rate and oxygen saturation trends in relation to interventions performed during the resuscitation. Without preparation and simulation, it is likely that the delivery room outcome may have been different.

9. Conclusions

Anticipation and preparation for DR emergencies are critical to the successful resuscitation of the high-risk newborn. DR emergencies are often unanticipated. Establishing a shared mental model at critical timepoints before (using a pre-brief), during (using a recap) and after (using a de-brief) resuscitation builds a foundation for effective team management. By leveraging the shared expertise and opinions of all members, the neonatal resuscitation team will more rapidly identify and manage emergencies.

When DR emergencies can be anticipated, such as in the case of the high-risk fetus with identified anomalies, multi-disciplinary collaboration is vital to the anticipation and preparation for potential interventions. In either scenario, the regular review of resuscitations, and the use of simulation to provide a forum for mastery learning and preparation, are fundamental to effective team management and efficient resuscitation in DR emergencies.

Practice points

- Anticipation and preparation are essential to effective management of DR emergencies.
- A shared mental model optimizes communication and collaboration across multi-disciplinary teams.
- A framework of dialogue, checklists, pre-briefing, recaps and debriefing ensure a shared mental model is maintained from pre-delivery preparation through post-resuscitation stabilization.
- Use of regular resuscitation review is critical to ensuring ongoing quality improvement of neonatal resuscitation programs.
- Simulation should be utilized to prepare for unanticipated and anticipated delivery room emergencies.

Research directions

- Assessment of barriers to optimal team functioning in DR emergencies.
- Determine the optimal method of training individuals and teams to maintain shared mental models in emergency situations.

Conflict of interest statement

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Delivery room emergencies: Respiratory emergencies in the DR

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ABSTRACT

The majority of newborns transition to extra uterine life without support. However, respiratory emergencies in the delivery room are a common occurrence. Whilst some situations are predictable e.g. the anticipated birth of an extremely preterm infant, others are less so. In this chapter we address the most frequent scenarios that result in delivery room respiratory emergencies and discuss the latest recommendations for their management. We outline the need for a trained resuscitation team and appropriate equipment to provide respiratory support at every birth. We address the basic care that all infants should receive, the detailed application of non–invasive ventilation and the use of advanced airway techniques. We discuss the unique challenges presented by extreme prematurity including umbilical cord management, use of supplemental oxygen, initial modes of respiratory support and surfactant delivery. We will explore optimal techniques in the management of infants with lung hypoplasia, pneumothorax and meconium aspiration.

1. Why are there respiratory emergencies in the delivery room (DR)?

Most newborn infants transition smoothly to extra uterine life. However, the need for respiratory support immediately after birth remains a relatively frequent neonatal emergency. Up to 5% of term-born infants need help to establish breathing [1], and although many very preterm infants have good initial respiratory efforts [2], the most premature infants are likely to need assistance to support and maintain their efforts [2]. The majority of delivery room respiratory emergencies therefore occur when infants don't breathe (mostly asphyxiated term infants), and in infants who cannot breathe sufficiently, mostly very preterm infants. Other emergencies occur in infants whose lungs are hypoplastic, who become unexpectedly unwell in the DR e.g. those who develop a pneumothorax or are born through meconium-stained amniotic fluid, and those who have anatomical anomalies (see Chapter *).

The key to successfully establishing breathing after birth is lung aeration. Inspiration, followed by prolonged expiration through a partly closed glottis drives lung fluid distally [3], the lungs aerate, functional residual capacity is established, pulmonary vascular resistance falls and pulmonary blood flow increases, perfusing the myocardium and increasing cardiac output [3]. Transition is facilitated by delaying cord clamping until after lung aeration: this delay stabilizes cardiac output and heart rate, maintaining left ventricular preload whilst the lungs aerate [4]. This sequence underlines why newborn resuscitation guidelines are heavily focused on respiratory support; when lung aeration is successful, gas exchange quickly results in a rising heart rate, meaning that for most newborn infants respiratory support is only briefly needed [5].

2. How do we recognize those in need of respiratory support in the DR?

Many DR respiratory emergencies can be predicted. The likelihood of needing respiratory support at birth increases in the presence of risk factors including placental abruption, cord prolapse or lower gestational age [6]. Nevertheless, respiratory emergencies frequently occur without clear antecedent events.

After birth, warming, drying, stimulating and opening the airway should occur [1] whilst assessments are made of tone, color, responsiveness, respiratory effort and heart rate (a key early sign of an infant's condition). Those with good tone and heart rate are unlikely to be severely hypoxic. In contrast, a pale, floppy baby who is apneic or bradycardic urgently requires positive pressure ventilation, ideally within 60 s [1]; to maximize the likelihood of success. Hence, positive pressure ventilation is the most important skill in neonatal resuscitation; all clinicians involved in stabilization at birth must be competent in the technique.

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As respiratory emergencies are unpredictable, every maternity center should have a fully trained resuscitation team and equipment for positive pressure ventilation immediately available. All healthcare providers involved with newborns must be regularly trained in newborn resuscitation. As knowledge and skills quickly decline [7], short, regular, low fidelity sessions are needed for optimal skill retention [8]. Team training is critical; poor teamwork and communication are the commonest causes of potentially preventable deaths in the DR [9], and team simulation training improves resuscitation outcomes [10]. Resuscitation team members need defined roles and an identified leader who directs, delegates and maintains situational awareness. A pre-resuscitation briefing that summarizes the scenario, identifies the roles, and plans the response should occur. A standardized pre-birth checklist enhances this preparation [11].

3. Practical management of respiratory emergencies

3.1. *Monitoring, thermoregulation, stimulation and supplemental oxygen*

During respiratory emergencies, monitoring of heart rate (by auscultation) and breathing effort should be undertaken. Where advanced technologies are available, pulse oximetry and electrocardiography are recommended [1]. Normothermia should be maintained, particularly in very preterm infants [12] in whom hypothermia is associated with increased mortality. A warmed room, radiant heat, and plastic wraps and hats are recommended [13]. Use of heated, humidified resuscitation gases should be considered [14]. Positioning, drying and stimulating is often sufficient to initiate spontaneous breathing in term infants, but if not, additional stimulation including rubbing the back, chest or abdomen, or flicking the foot may be helpful. These interventions are often delayed or omitted [15] and experts have suggested that, on a global scale, immediate neonatal assessment with stimulation could reduce peri-partum deaths by 10% [16].

When there is an inadequate response, positive pressure ventilation (PPV) is required without delay. For term infants, resuscitation should commence in 21% oxygen, except if cardiac compressions are required when 100% oxygen is suggested [1]. For preterm infants, supplemental oxygen is probably necessary [1]; 30% oxygen is frequently recommended although evidence is inconclusive [17]. Whatever oxygen concentration is initiated, this should be titrated against targets based on the rising saturations of normal term infants in the minutes following birth [18].

3.2. *Respiratory support*

Newborns who fail to respond to basic measures require positive pressure support. This is typically applied using a facemask or nasal prong(s) and a pressure-generating device. When some respiratory effort is present, continuous positive airway pressure (CPAP) may be sufficient to support lung aeration and functional residual capacity. However, an apneic or bradycardic infant requires positive pressure ventilation (PPV).

3.2.1. *Generating positive pressure*

Several devices can be used to deliver PPV. These vary in terms of their cost, need for a gas supply and ability to deliver PEEP/CPAP. Self-inflating bags (SIBs) are widely available and can be used without a gas supply, making them the most useful device in resource-limited settings. Delivered pressures and volumes vary with how much the bag is squeezed, although the latest “upright” designs of SIB provide more consistent volumes [19]. SIBs can be fitted with attachments that allow them to deliver PEEP, but not CPAP. Flow-inflating bags (FIBs) need a continuous gas supply to re-expand, again delivered pressures and volumes vary depending on how much the bag is squeezed, and FIBs may be more difficult to use than SIBs [20]. Attachments can be used to support PEEP delivery, but consistent PEEP is difficult to achieve. Neither device is optimal for preterm infants who need CPAP and/or PEEP [21].

The T-piece device is a popular alternative. It is a flow-controlled system, requiring a gas supply, but with the advantage of being able to set desired pressures. T-pieces accurately deliver peak inspiratory pressure (PIP), PEEP and CPAP, with less tidal volume variability than other devices [22], and they are preferred by clinicians [23]. However, studies have not shown important differences in outcomes between devices [24]. If either a T-piece or FIB is preferred, a back-up SIB should be available in case of failure of gas supply. Safe and effective ventilation during neonatal resuscitation depends on delivery of sufficient tidal volume to exchange oxygen and carbon dioxide without causing lung damage through volutrauma. However, none of these devices measure tidal volume. Although it is feasible to monitor volume delivery in the DR [25], the devices are yet to be tested in large randomized controlled trials (RCTs). Neonatal ventilators can provide accurate pressure and volume delivery, as well as CPAP/PEEP [26], but they are expensive and require training and practice to use correctly.

3.2.2. *Pressure, volume and timing of mask ventilation*

When respiratory efforts are either absent or inadequate, PPV is required for clearance of lung liquid and aeration. In term infants, the focus is on rapid assessment with brief stimulation, followed quickly by lung aeration using positive pressure in room air, supported by PEEP where available.

PPV is typically delivered via a circular mask covering the mouth and nose. During PPV, inflation rates of 40–60 per minute are recommended, with duration of each inflation timed to reflect spontaneous inspiratory times of newborns (about 0.3 s) [27]. Effective mask ventilation requires a good seal between the mask and the infant's face [28] whilst minimizing mask leak and airway obstruction. Effective mask technique is difficult to achieve and maintain [20]. Masks of the correct size and shape are needed, along with correct placement and hold. Using a mask and T-piece, operators typically have 40–60% leak [28]; when leak rises further, delivered pressures and volumes fall [29]. Neither peak pressure nor chest rise are good indicators of delivered volume [30]. Colorimetric carbon dioxide detectors may be used to confirm volume delivery and determine effectiveness of ventilation [31], responding before improvements in heart rate and oxygen saturations [32]. Concern over mask leak can result in excessive mask pressure being applied [33], distorting the nose, obstructing the airway [29, 34] and impeding effective mask ventilation. Simply placing a mask over the face can result in reflex apnea requiring escalation in resuscitative efforts. This effect has driven the search for alternative interfaces, such as a nasally placed cut-down endotracheal tube [35], short bi-nasal prongs [36] and nasal cannulae [37, 38]. However, none of these have been shown to be superior to a facemask in an RCT.

During mask ventilation, tidal volume delivery depends on multiple factors; spontaneous breathing effort, glottic opening, lung compliance, applied pressures, mask leak and airway obstruction. This results in delivery of variable tidal volumes, often much higher than volumes generated during spontaneous breathing [39], risking lung and brain injury [40]. Guidelines recommend starting with peak pressures of 20–30 cm H_2O [1], as these typically produce adequate, but not excessive, tidal volumes. PEEP is routinely provided for term and preterm infants during resuscitation despite the lack of strong clinical evidence of its effectiveness in the DR. There is convincing animal evidence of benefit for PEEP in establishing functional residual capacity [21] meaning that it is recommended for preterm infants and reasonable for term infants [1]. A single, standard level of PEEP is unlikely to suit all preterm infants, those with the highest oxygen requirements may require higher PEEP.

During mask ventilation, if chest wall movement is poor or absent, steps need to be taken to ensure optimal mask size, positioning and hold, and PIP may need to be increased [41]. Once the heart rate is above 100 beats/minute and spontaneous breathing is established, PPV can be ceased in term infants, or converted to mask CPAP in preterm infants.

3.2.3. Advanced airway support

Infants who do not respond to PPV (heart rate < 100 beats/minute after 30 s of effective mask ventilation), may require endotracheal intubation. Other indications for intubation include persistent hypoxia despite mask ventilation, or a prolonged need for mask ventilation [1]. The decision to intubate may vary according to gestational age, respiratory effort, and experience of the resuscitator.

Neonatal intubation is a technically challenging procedure. With changes in practice, fewer infants are being intubated. It is increasingly difficult to train junior clinicians to perform the task, and skills are declining. Experienced operators successfully intubate at the first attempt more than 85% of the time, whereas junior trainees succeed less than half the time [42], frequently taking longer than the recommended 30 s [42]. Rates of successful intubation can be improved by the use of videolaryngoscopy supervised by an experienced intubator [43].

Alternative airway adjuncts, such as a laryngeal mask airway (LMA), may be useful, particularly for less experienced clinicians. LMAs are quick and easy to insert [44]; even for novices success rates are high. LMAs are commonly used in neonatal anesthesia and have been trialled successfully at birth in settings where resources, training and experience are limited [45]. Guidelines recommend that LMAs should be available in all birth settings and neonatal resuscitators should be trained in their use. They may be life-saving when mask ventilation is unsuccessful and endotracheal intubation is not possible [1]. However, there are a limited range of LMA sizes available, and their use is not usually possible in infants below 1500 g, or 31 weeks' gestation. Whichever method is used to achieve ventilation, lung aeration must be established before commencement of chest compressions, as compressions will be ineffective without lung aeration.

4. Special situations

4.1. The extremely preterm infant

Extremely preterm infants born < 28 weeks' gestation represent a unique and high-risk patient group. Optimal antenatal care, including antenatal corticosteroids and magnesium sulfate, tocolysis, and transfer to a tertiary-level center when possible improves outcome [46]. Extremely preterm infants have immature, surfactant-deplete lungs and almost universally require some respiratory support, both for apnea and for respiratory distress syndrome (RDS); they much more frequently require advanced resuscitation interventions such as endotracheal intubation compared with more mature infants. Their stabilization in the DR requires careful and tailored management that aims to minimize lung injury and optimize longer-term outcomes.

4.1.1. Umbilical cord clamping

The benefits of delayed cord clamping (DCC) in mature infants are well documented, and these benefits may also apply to extremely preterm infants. Although no difference was seen in a recent large trial of DCC in infants born < 30 weeks' gestation [47], a recent meta-analysis of trials comparing DCC with immediate clamping showed a significant reduction in mortality before hospital discharge when DCC was used, including in the extremely preterm subgroup [48]. DCC in extremely preterm infants has additional challenges, including access to the infant to provide respiratory support, and temperature control. Specialized equipment has been developed and tested to make DCC in these infants feasible [49], and is under investigation. Currently, clinicians wishing to provide DCC to this group typically only do so if the infant is assessed as not requiring immediate respiratory intervention. Umbilical cord 'milking' is another technique recently investigated [50]. However, an association with intra-ventricular hemorrhage means it currently cannot be recommended [51].

4.1.2. Apnea

Most extremely preterm infants will demonstrate respiratory effort soon after birth [2]. If not, like more mature infants, they should be stimulated. However, in the rush to initiate respiratory support this step is sometimes forgotten in the smallest infants [52]. Caffeine is a respiratory stimulant routinely used to treat extremely preterm infants in the neonatal unit, based on extensive evidence of short- and long-term benefits [53, 54]. Caffeine in the DR is feasible and may be beneficial [55], but more research is required.

4.1.3. Supplemental oxygen

In the minutes after the birth of an extremely preterm infant, clinicians must balance the need for adequate oxygenation with the avoidance of hyperoxic damage to developing organs such as the brain and retina. Titrating supplemental oxygen against peripheral oxygen saturations is recommended, although data on the optimal targets are limited in this population. In extremely preterm infants, resuscitation with 21% oxygen may be disadvantageous compared with using 100% oxygen in terms of poorer recovery from bradycardia and higher mortality [56]. However, no significant differences were seen in a meta-analysis of RCTs comparing lower (≤30%) with higher (≥60%) oxygen for infants born < 29 weeks' gestation [57]. Guidelines currently recommend commencing extremely preterm infants in some (21–30%) oxygen,[1 46] indicating a preference to minimize exposure to supplemental oxygen in the absence of convincing evidence of benefit from higher concentrations.

4.1.4. Respiratory support

It has been hypothesized that quickly establishing adequate lung volume in the DR by using sustained inflations may reduce lung injury in extremely preterm infants. Whilst early trials showed promising improvements in short-term outcomes [58], a large, recent RCT did not support this and was stopped early due to an increase in early deaths (within 48 h of birth) in the intervention group [59].

Historically, extremely preterm infants were routinely managed with early endotracheal intubation in the DR. However, meta-analysis of the four large RCTs comparing early nasal CPAP with routine endotracheal intubation [60] found a borderline reduction in BPD in the CPAP group, no difference in mortality, and a significant benefit for the combined outcome of death or BPD at 36 weeks' PMA in the CPAP group. Given these findings, clinicians increasingly attempt to stabilize extremely preterm infants without an endotracheal tube.

4.1.5. Surfactant

Early respiratory management of extremely preterm infants aims to avoid intubation and ventilation, whilst identifying the need for surfactant and administering it as early as possible when required. Early surfactant administration decreases the risk of mortality, BPD, and pulmonary air leaks [61], and the only benefit to delaying surfactant administration is to avoid intubation. Requirement for surfactant in the DR is assessed clinically, using oxygen requirement, level of respiratory distress and response to resuscitation as guides. Point-of-care lung ultrasound and rapid quantification of surfactant in gastric aspirates to assess the need for surfactant remain under investigation.

Endotracheal surfactant administration requires intubation skills and availability of mechanical ventilation. Surfactant administration without intubation (less- or minimally-invasive surfactant administration), given via a thin catheter during spontaneously breathing on CPAP, has been developed and tested. Meta-analysis of RCTs of the technique suggest that it is superior to endotracheal administration; reducing the need for mechanical ventilation and the combined outcome of death or BPD [62]. These less-invasive techniques still require laryngoscopy and debate continues as to the appropriate analgesia required to avoid distress and maintain physiological stability [63]. Techniques that avoid laryngoscopy, such as pharyngeal instillation [64], nebulisation [65], and administration via an LMA [66], are under investigation but none are yet ready for clinical use.

4.2. Pneumothorax

Leakage of air following rupture of overdistended alveoli tracks to the pleura causing pneumothorax. Although the condition may occur in healthy term infants receiving no resuscitation, it is more commonly associated with other pathologies including meconium aspiration syndrome, surfactant deficiency and pulmonary hypoplasia, usually in conjunction with PPV. In the DR, pneumothorax may present as a sudden deterioration in an infant's condition manifested by hypoxemia, poor perfusion, reduced breath sounds and asymmetry or overdistension of the chest wall. Rapid diagnosis using transillumination, and confirmation with a chest x-ray prior to drainage is ideal but when an infant is unstable, treatment should proceed immediately. Point-of-care lung ultrasound has recently been demonstrated to reliably diagnose pneumothorax in the NICU [67] and may be applicable in the DR. Conventional treatment involves placement of a chest tube, positioned anterior to the affected lung, this can be challenging in the DR where asepsis may be harder to attain. Recent data show that in the NICU initial needle aspiration adequately treats pneumothorax in 30% of cases [68]. The applicability of this technique in the DR is untested.

4.3. Meconium stained amniotic fluid (MSAF)

MSAF is an indication of fetal distress and a risk factor for the need for respiratory support after birth. Therefore, a trained resuscitator with intubation skills should attend births complicated by MSAF. The approach to MSAF has become less aggressive over the past two decades. Routine oropharyngeal or tracheal suctioning of vigorous infants born through MSAF is not beneficial [69, 70]. The question of how best to manage the non-vigorous infant remains controversial. A small RCT showed no reduction in incidence of meconium aspiration syndrome or other adverse outcomes with routine intubation and tracheal suction [71]. This lack of effectiveness, and the potential delay in providing mask ventilation, led the International Liaison Committee on Resuscitation to state that there is insufficient evidence to support routine suctioning of meconium in non-vigorous infants born through MSAF [1], but that large RCTs are needed to better answer this important question.

4.4. Lung hypoplasia

A variety of conditions are associated with poor lung growth including congenital diaphragmatic hernia, dealt with in Chapter *. Lack of lung fluid during fetal development, such as from prolonged preterm rupture of the membranes (PPROM) with reduced amniotic fluid volume leads to immature, hypoplastic lungs [72]. Outcomes following PPROM have improved over the last 20 years as surfactant, inhaled nitric oxide to manage pulmonary hypertension, high frequency oscillatory ventilation and cardiovascular support agents have been more consistently offered. Survival rates have improved substantially, up to 90% in recent reports [73]. Therefore, full resuscitation efforts in the DR should be initiated, directed at minimizing further lung damage. Hypoplastic lungs often have normal compliance. Therefore, the use of low distending pressures to avoid lung damage and cardiovascular compromise is appropriate [74]. Pneumothorax is more frequent and a sudden deterioration should alert clinicians to look for and treat this potential complication. Once stabilized, consideration should be given to early detection and treatment of surfactant deficiency and pulmonary hypertension.

5. Summary

Most newborn infants do not require intervention to successfully transition to extra uterine life. However, on a global scale, efficient stabilization and resuscitation of all newborn infants who need help to establish breathing at birth, particularly asphyxiated term infants would save many lives. The provision of effective ventilation in the DR is key to achieving this goal.

Practice points

- DR respiratory emergencies are common and not always predictable.
- All centers where births occur should have staff who are trained and prepared to deliver immediate respiratory support.
- For all infants, focusing on lung inflation with timely and continuous respiratory support is critical.
- In term infants, resuscitation should commence using air; the commonest pathologies to consider are asphyxia, meconium aspiration, lung hypoplasia and pneumothorax.

Research directions

- The optimal concentration of oxygen and target oxygen saturation levels during resuscitation of preterm infants need to be established.
- The role of commencing respiratory support before umbilical cord clamping needs evaluation.
- The optimal training regimes to achieve and maintain resuscitation skills need to be identified.

Declaration of competing interest

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Circulatory emergencies in the delivery room

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ABSTRACT

The transition from fetal to neonatal life is a dramatic and complex process involving extensive physiologic changes, which are most obvious at the time of birth. Individuals who care for newly born infants must monitor the progress of the transition and be prepared to intervene when necessary. In the majority of births, this transition occurs without a requirement for any significant assistance. If newborns require assistance, the majority of the time respiratory support is all that is required. In some instances, however, there are circulatory emergencies that need to be rapidly identified or there may be dire consequences including death in the delivery room. This chapter will review various pathologies that are circulatory emergencies, and discuss how to assess them. We will also review new technologies which may help providers better understand the circulatory status or hemodynamic changes in the delivery room including heart rate, cardiac output, cerebral oxygenation and echocardiography.

1. Normal transitional changes in circulation

In order to better understand abnormal circulation, it is important to understand the normal transition from fetal to neonatal circulation (Fig. 1, **Panel A and B**). Fetal circulation begins with blood entering the fetus from the placenta through the umbilical vein. The blood is directed towards the left ventricle with shunting across the foramen ovale and ductus arteriosus. Pulmonary blood flow is decreased with constricted pulmonary arteries due to low alveolar oxygen and lung liquid. With the clamping of the umbilical cord, the placenta with its low vascular resistance is removed from the neonatal circulation, resulting in a rise in neonatal systemic blood pressure. At the same time, lung expansion results in release of surfactant and absorption of lung liquid increasing pulmonary blood flow.

These two changes decrease the fetal right-to-left shunt at the ductus arteriosus, resulting in an increasing left-to-right shunt at the ductus arteriosus. Ventilation of the lungs also results in increased blood flow through the pulmonary arteries and lungs. This shift to left-to-right shunting after delivery results in an increase in ventricular stroke volume, which is associated with an increase in cerebral oxygen saturation. With increased lung perfusion and expansion, neonatal oxygenation saturation is increased, which stimulates closure of the ductus arteriosus.

In addition, the increased pulmonary arterial blood flow raises pulmonary venous return to the left atrium and increases left atrial pressure. As the left atrial pressure increases and the right atrial pressure falls, right-to-left shunting across the foramen ovale decreases. Closure of the foramen ovale occurs when the left atrial pressure exceeds the right atrial pressure. Clinically these manifest as a newborn with increasing heart rate and improvement in color and perfusion over the first several minutes after birth.

2. Circulatory emergencies in newborns

Healthy newborns complete the transition from intrauterine to extra-uterine life without difficulty, however about 10% of infants will have impairedadaptation [1]. The most important indicator of a successful transition is an increasing heart rate over the first few minutes. Once an infant has either established their own breathing or requires positive pressure ventilation, they typically have a rising or stable heart rate above 100 beats per minute. The majority of infants that do not have an increasing heart rate at birth are due to inadequate expansion of the lungs due to ineffective ventilation [1]. If an airway has been secured and proper endotracheal placement has been established to achieve effective ventilation of the lungs, persistence of bradycardia constitutes a circulatory emergency and the following conditions should be urgently considered.

Cardiac disease — Infants with severe congenital heart disease may have difficulty with the transition to extrauterine life. The most common are those with cyanotic heart disease who are dependent upon

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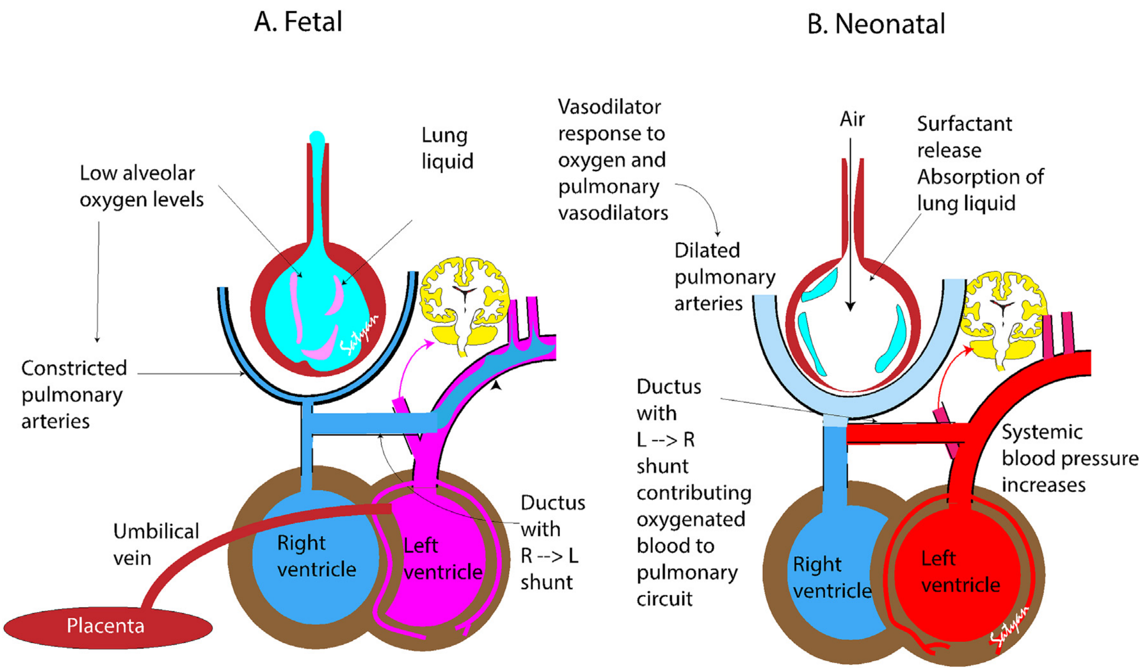

A. Fetal

B. Neonatal

Low alveolar oxygen levels
Lung liquid
Constricted pulmonary arteries
Umbilical vein
Placenta
Right ventricle
Left ventricle
Ductus with R --> L shunt
Vasodilator response to oxygen and pulmonary vasodilators
Dilated pulmonary arteries
Air
Surfactant release
Absorption of lung liquid
Ductus with L --> R shunt contributing oxygenated blood to pulmonary circuit
Systemic blood pressure increases
Right ventricle
Left ventricle

Fig. 1. Normal transition from fetal (panel A) to neonatal circulation. Copyright Dr. S. Lakshminrusimha, UC Davis.

a patent ductus arteriosus for pulmonary or systemic blood flow, or those with severe pulmonary edema due to increased pulmonary arterial blood flow or impaired left ventricular function. The majority of newborns with congenital heart disease do not present with major circulatory issues due to the presence of a patent ductus arteriosus. However, if a closed or restrictive patent ductus is suspected, the clinical team should be prepared to place IV access shortly after birth and administer prostaglandin to ensure ductal patency for critical left and right sided obstructive lesions [1]. Rarely transposition with an intact or restrictive atrial septum can require urgent transport to the catheterization laboratory or even bedside septostomy to ensure adequate atrial mixture.

2.1. Pneumothorax, pneumomediastinum or pneumopericardium

Of all of the circulatory emergencies that occur in the delivery room those involving the lungs are the most common and emergent. Pneumothorax occurs more commonly in the newborn period than at any other time. Newborns between 30 and 36 weeks of gestational age or term infants delivered by cesarean section, newborns with meconium aspiration syndrome and those infants requiring extensive resuscitation have an increased risk of pneumothorax. Spontaneous pneumothorax also can occur in a newborn that has not required any resuscitation. The incidence of pneumothorax ranges from 0.07 to 3% [2]. Most air leaks are found in asymptomatic babies who underwent a radiographic examination of the chest as part of a screening series.

Some infants may present with respiratory distress, grunting, nasal flaring, retractions, and tachypnea. There may be asymmetric chest movement but this may not be readily detected. If pneumothorax is large enough, heart sounds may be shifted. Auscultation may reveal decreased breath sounds on the affected side, although normal breath sounds may result from easily transmitted sounds from the contralateral side. In smaller premature infants transillumination of the chest should be considered. If there is bradycardia and/or hypoxia, measures should be undertaken immediately to drain the air (see Fig. 2).

When air is obtained, it is evacuated with the syringe, usually resulting in improvement in the infant's condition. If there is no improvement, one should consider the possibility of a contralateral pneumothorax, requiring drainage. Following stabilization, a decision must be made regarding further therapy. If the infant appears well with no underlying lung disease, no need for mechanical ventilation, and no reaccumulation of the pneumothorax, observation generally is all that is required. If any of these criteria are not fulfilled, it may be necessary to insert a thoracotomy tube for continuous drainage of the intrapleural air. If signs of respiratory distress are present but evaluation allows pneumothorax to be excluded, other types of air leak should be suspected.

Pneumomediastinum occurs with a reported incidence of 25 per 10,000 births in similar circumstances as pneumothorax. The signs and symptoms are generally less severe, and are often limited to tachypnea or mild flaring and retractions [3]. At times, the sternum may appear bulging. Auscultation will reveal distant heart sounds. Treatment generally is limited to careful observation, with aggressive intervention rarely required.

Rarely in the delivery room an infant can present with a pneumopericardium. Clinical features of this air leak include the sudden development of cyanosis, muffled heart sounds, and decreased blood pressure [4]. The severity of this condition varies from asymptomatic to life threatening, and several authors have recommended conservative management unless signs of tamponade are seen. The suspicion of this condition in a newborn whose critical state has not been improved by other therapies mandates rapid pericardiocentesis to reestablish cardiac output. This procedure is described in Fig. 3.

At least half of infants with pneumopericardium will require repeat aspiration, in which case the placement of an indwelling tube with continuous drainage is advocated.

2.2. Hydrops

Hydrops fetalis represents a severe condition that generally results in depression of the infant at birth and requires immediate coordinated action in the delivery room. This condition is characterized by total body edema, often with associated collections of fluid in the pleural, pericardial, and peritoneal spaces [5]. Most cases seen today are unrelated to Rh or other blood group isoimmunization, and have a non-immune etiology. The causes include hematologic conditions causing anemia, structural heart disease or rhythm disturbances causing congestive heart failure, various congenital infections, as well as

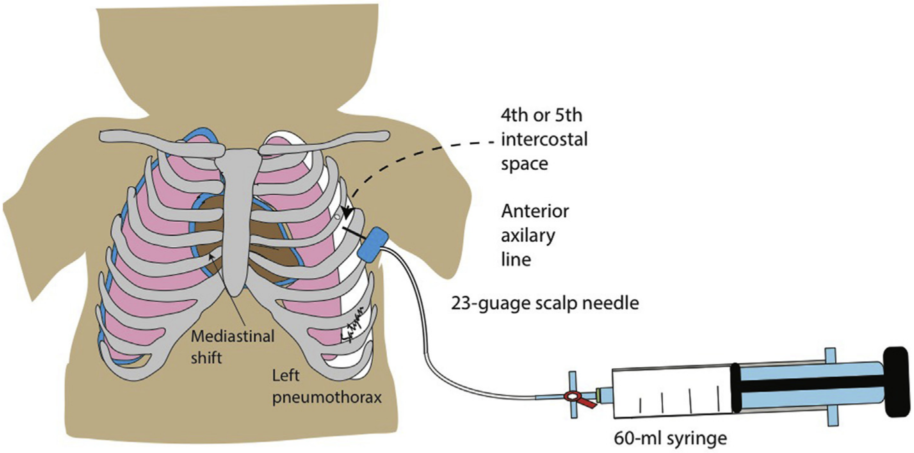

Fig. 2. Treatment of Pneumothorax with needle aspiration. Copyright Dr. S. Lakshminrusimha, UC Davis.

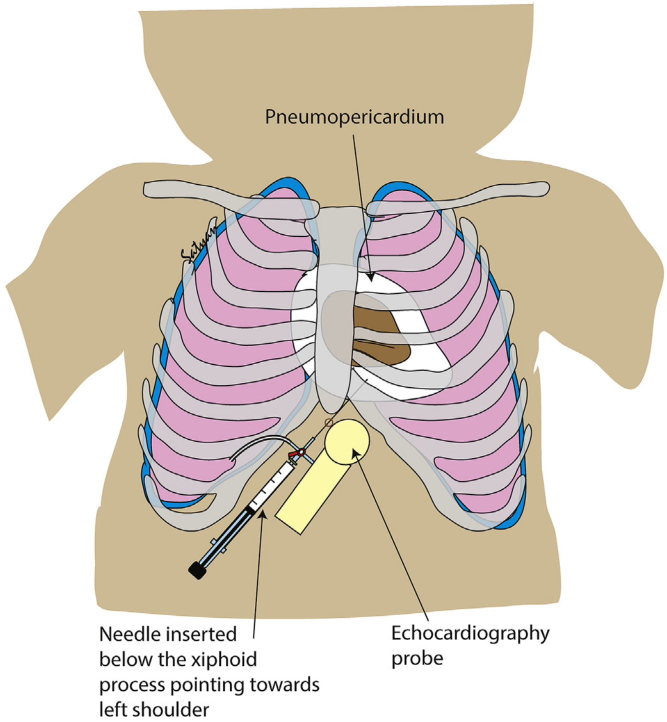

Fig. 3. Treatment of Pneumopericadium with needle aspiration. Copyright Dr. S. Lakshminrusimha, UC Davis.

malformations and chromosomal abnormalities. No single mechanism explains pathogenesis in these conditions. The presence of prematurity, congenital anomalies, or chromosomal disorders has been associated with a diminished prognosis while hydrops due to cardiac arrhythmias has a better outlook. Cases of hydrops related to supraventricular tachycardia have been corrected in utero through maternal treatment with digitalis. In all cases, complete prenatal diagnosis has played a major role in improved survival. The delivery of a hydropic infant should be attended by a team of pediatricians. If prenatal diagnosis or postnatal assessment suggests large effusions, more than one person will be necessary to accomplish rapid and effective resuscitation. Following the general guidelines of resuscitation, the hydropic infant in distress should be quickly intubated to allow rapid establishment of adequate oxygenation and ventilation. Team members should be assigned specific tasks, including central line placement, and drainage of pleural, peritoneal, or pericardial fluid. Diagnoses such as anemia known prenatally or diagnosed at birth, treatment with partial exchange transfusion with O-negative packed red blood cells can be accomplished through umbilical venous and arterial catheters. In any case, the stabilized infant can be taken to the newborn intensive care unit, where a complete evaluation of potential etiologies can be pursued.

2.3. *Fetal blood loss*

Placental abruption is defined as the premature detachment of the placenta from the uterine wall and occurs in 0.6%–1% of all pregnancies in the Unites States [6]. Placental abruption causes a decrease in the surface area available for oxygen exchange and nutrient and blood supply to the fetus. Newborns born with a placental abruption at delivery are at an elevated risk for neonatal resuscitation, asphyxia, and mortality.

Umbilical cord prolapse is another obstetrical emergency that can have significant neonatal morbidity and/or mortality. It is diagnosed by visualizing/palpating the prolapsed cord outside or within the vagina in addition to abnormal fetal heart rate patterns. Women at higher risk of umbilical cord prolapse include multiparous with malpresentation. Other risk factors include polyhydramnios and multiple pregnancies.

The majority of pregnancies have minimal hemorrhage of fetal blood into the maternal circulation. Rarely, the hemorrhage can be large enough to compromise the fetus resulting in demise, stillbirth, or delivery of a severely anemic infant. The symptoms of a significant fetal-maternal hemorrhage can be subtle, non-specific and difficult to identify. Prenatally the mother may present with a history of decreased or absent fetal movement [7]. Fetal heart rate monitoring will show a sinusoidal pattern, a lack of acceleration and recurrent late decelerations [8]. A sinusoidal fetal heart rate pattern is a category III classification necessitating immediate assessment [9].

Cord avulsion or spontaneous umbilical cord rupture is defined as the disruption of one or more of the umbilical cord vessels at some point between the fetus and the placenta [10]. Significant blood loss can occur and rapid intervention may be necessary to prevent perinatal morbidity and mortality. The majority of cases have been in the setting of patients with a velamentous cord insertion or in the setting of a difficult extraction.

3. Assisting circulation

In newborn infants the need for resuscitative measures beyond assisted ventilation is extremely rare. Additional circulatory assistance can include chest compressions, administration of epinephrine, and volume infusion. In a large urban delivery center with a resuscitation registry, 0.12% of all infants delivered received chest compressions

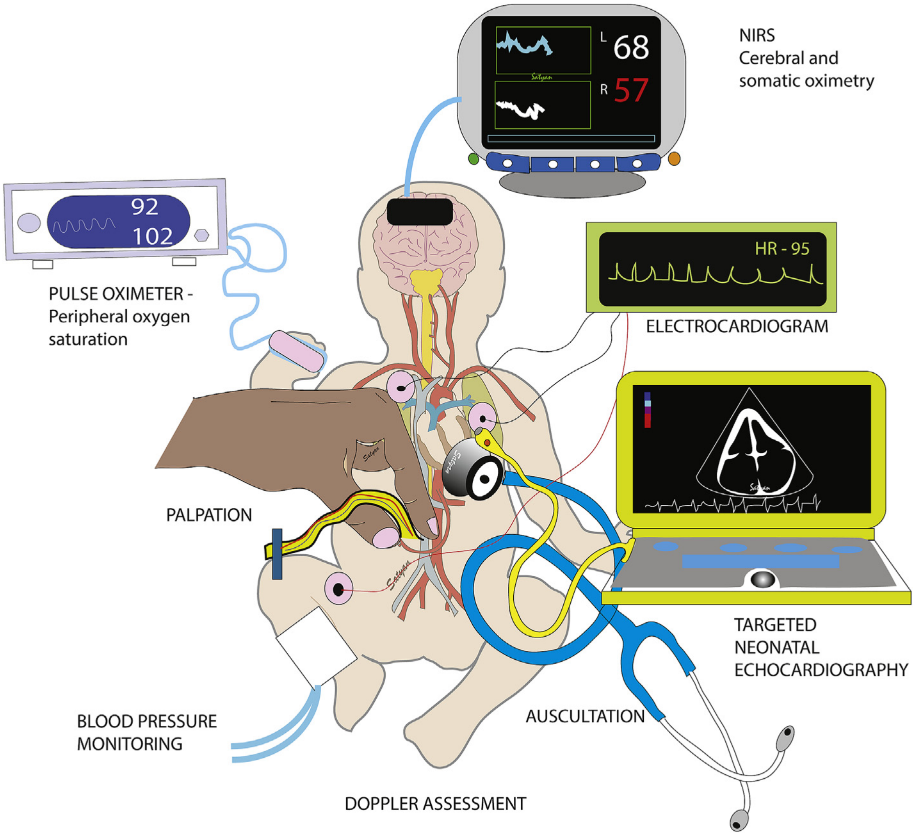

Fig. 4. Methods for circulatory assessment in the delivery room. Copyright Dr. S. Lakshminrusimha, UC Davis.

and/or epinephrine in 1991–1993 [11] and 0.06% of all infants delivered received epinephrine from 1999 to 2004 [12]. Ventilation remains the most critical priority in neonatal resuscitation. However, if adequate ventilation is provided for 30 s, and bradycardia with heart rate < 60 bpm persists, chest compressions are initiated. Further attention to ventilation with the use of increased pressures and/or intubation may be required. Chest compressions are preferably provided with two thumbs on the sternum while both hands encircling the chest [13]. The chest is then compressed in a 3:1 ratio coordinated with ventilation breaths.

Further circulatory support may be necessary if adequate chest compressions and ventilation with 100% oxygen do not result in an increase in heart rate after 60 s. Epinephrine is then indicated as a vasoactive substance which increases blood pressure by alpha-receptor agonism, improves coronary perfusion pressure, and increases heart rate by beta-receptor agonism. Intravenous administration of epinephrine is more likely to be effective than endotracheal administration. The intravenous dose of 0.01–0.03 mg/kg (0.1–0.3 mL/kg of a 1:10,000 solution) is currently recommended. Early placement of an umbilical venous catheter is critical in order to deliver intravenous epinephrine quickly enough to be effective. In order to place an umbilical catheter as quickly as possible it is necessary to have the equipment readily available and to begin the procedure as soon as possible. This could be accomplished by the lead resuscitator assigning the task of placing the catheter as soon as chest compressions are initiated. If there is any prenatal indication that substantial resuscitation will be required, the necessary equipment for umbilical venous catheter placement should be prepared before delivery. Epinephrine may be given by endotracheal tube but the efficacy of this delivery method is not as certain and therefore an increased dose of 0.05–0.1 mg/kg (0.5 mL–1 mL/kg of a 1:10,000 solution) is currently recommended. Epinephrine doses may be repeated every 3 min if heart rate does not increase over 60 beats per minute. Excessive epinephrine may result in hypertension which in preterm infants may be a factor in the development of intraventricular hemorrhage. However, the risks are balanced by the benefit of successful resuscitation in an infant who might not otherwise survive.

If the infant has not responded to all of the prior measures a trial of increasing intravascular volume should be considered by the administration of crystalloid or blood. Situations associated with fetal blood loss are also frequently associated with the need for resuscitation. These include placental abruption, cord prolapse, and fetal maternal transfusion. Some of these clinical circumstances will have an obvious history associated with blood loss whereas others may not be readily evident at the time of birth. Signs of hypovolemia in the newborn infant are non-specific but include pallor and weak pulses. Volume replacement requires intravenous access for which emergent placement of an umbilical venous catheter is essential. Any infant who has signs of hypovolemia and has not responded quickly to other resuscitative measures should have an umbilical venous line placed and volume infusion administered. The most common (and currently recommended) fluid for volume replacement is isotonic saline. A trial volume of 10 mL/kg is given initially and repeated if necessary. If a substantial blood loss has occurred the infant may require infusion of red blood cells to provide adequate oxygen carrying capacity. This can be accomplished emergently with non-crossmatched o-negative blood, with blood collected from the placenta, or with blood drawn from the mother who will have a compatible antibody profile with her infant at the time of birth. Because not all blood loss is obvious and resuscitation algorithms usually include volume replacement as a last resort of a difficult resuscitation, the clinician needs to keep a high index of suspicion for significant hypovolemia so that action may be taken to correct the problem as promptly as possible. Therefore, in situations where the possibility for hypovolemia and need for placental transfusion is known prior to birth it is important to prepare an umbilical catheter, a syringe with isotonic saline and discuss with the blood bank and the delivering physicians the possibility that non-crossmatched blood may be required.

4. Assessing circulation- EKG, NIRS, cardiac output monitoring, echocardiography

There are a number of methods for circulatory assessment (see Fig. 4).

Just as fetal heart rate monitoring can be valuable in identifying emergent perinatal problems such as a prolapsed umbilical cord or asphyxia, heart rate (HR) is the most important clinical indicator to evaluate the overall status of a newborn and is also used to guide any resuscitation efforts. Several studies have demonstrated that HR by auscultation or palpation of the umbilical cord are inaccurate [14–16]. Heart rate from a hand held Doppler correlates reasonably well with electrocardiogram (EKG) and pulse oximetry (PO) heart rates [15,17]. Smartphone based pulse rate applications have also been evaluated [18]. These methods are also most commonly done only for a few seconds at a time and require that an individual stop other procedures to conduct a brief evaluation of heart rate at a time when heart rate and cardiovascular status are in continuous flux. For this reason, continuous heart rate measurements In general are superior to auscultation and palpation. Continuous pulse rate from a pulse oximeter is comparable to that of EKG, but there is an initial stabilization period where the HR may be inaccurate until an adequate wave form is achieved [19]. Several non-contact methods are currently under investigation but are not readily available as a tool to collect continuous HR data, including photoplethysmography and non-contact Doppler radar [20–22]. EKG is a proven technology that provides a reliable HR faster than pulse oximetry [19,23,24]. In addition, one study has shown that pulse oximetry in the first 2 min of life frequently displayed the newborn's HR below 60 beats per minute, while a simultaneous EKG showed the HR greater than 100 beats per minute [25]. The recent guidelines from the International Liaison Committee on Resuscitation recommend the use of a 3-lead EKG for rapid and accurate assessment of a newborn's HR.

Recently, there have been novel tools used in the NICU that are now being studied in the delivery room to monitor the circulatory status of the newborn. The rationale for this is that there may be the potential to identify a circulatory emergency sooner or restore circulation adequately with additional monitoring. The non-invasive nature of these modalities make them ideally suited for the delivery room where central access and other invasive methods may be too time consuming and labor intensive during a resuscitation.

Preterm infants that require extensive resuscitation at birth have a higher rate of intraventricular hemorrhage (IVH) and death [26]. Current methods of monitoring a premature newborn at birth include HR and peripheral arterial oxygen saturation (SpO_2). Neither allows direct assessment of the brain at birth. Non-invasive neural monitoring by Near Infrared Spectroscopy (NIRS) and amplitude integrated electroencephalography (aEEG) has been show to detect differences in early brain injury [27–29]. NIRS may allow for detection of low regional blood flow earlier than blood pressure, lactate, or urine output.

Monitoring in the neonatal intensive care unit (NICU), may include neuromonitoring with aEEG and/or cerebral oxygenation with NIRS. However, monitoring in the delivery room remains minimal. Cerebral oxygenation and aEEG monitoring at birth may predict infants at risk for poor outcomes. A few trials have attempted to bring both aEEG and NIRS into the delivery room but only for monitoring near-term and term infants, many of whom did not require any resuscitation [30,31]. Delivery room monitoring of preterm infants during resuscitation may lead to an improved understanding of how the premature brain responds during this critical time and provide physiological basis for changes in the resuscitation process. These very early, potentially corrective changes in physiology may be able to protect the brain from permanent injury.

Cardiac output monitoring allows for continuous monitoring during transition. One method uses electrical velocimetry to non-invasively measure stroke volume, cardiac output and heart rate using 4 surface EKG electrodes. Two studies have used this technology in the delivery room, one in term infants during vaginal birth with delayed cord clamping [32] and the other was at Cesarean section after the cord was clamped and cut [33]. This technology needs further validation due to its poor correlation with transthoracic echocardiography [34].

Functional echocardiography may allow adopting a physiology-based targeted intervention in sick infants with hemodynamic instability – treating low preload states with volume resuscitation. Bedside echocardiography can be used to assess cardiac function. The systolic function of the left ventricle can be quickly assessed on visual inspection by 'eye-balling' the contractility, or quantitatively by measuring the shortening fraction on M-mode. Pericardial effusion can be easily recognized on functional echocardiography, and a timely intervention in presence of cardiac tamponade may improve outcomes.

Echocardiography in the delivery room can provide a real time assessment of cardiac output and hemodynamics [35]. A study completed by Noori et al. demonstrated significant changes in cardiac function, cerebral hemodynamics and oxygenation in 20 subjects in the delivery room. While requiring a significant amount of expertise and training, the increasing number of neonatologists trained to perform cardiac ultrasounds may allow its use to become more common in the near future.

Practice points

- Timely identification of circulatory emergencies is critical in the delivery room
- Preparation of a circulatory emergency should include correct personnel and equipment.
- Newer modalities such as NIRS and echocardiography may improve timely diagnosis of circulatory emergencies but this needs further study.

Conflict of interest

None of the authors have any conflicts.

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Delivery room emergencies in critical congenital heart diseases

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ABSTRACT

Transition from fetal to postnatal life is a complex process. Even in the absence of congenital heart disease, about 4–10% of newborns require some form of assistance in the delivery room. Neonates with complex congenital heart disease should be expected to require significant intervention and thus the resuscitation team must be well prepared for such a delivery. Prenatal assessment including fetal and maternal health in general and detailed information on fetal heart structure, function and hemodynamics in particular are crucial for planning the delivery and resuscitation. In addition, understanding the impact of cardiac structural anomaly and associated altered blood flow on early postnatal transition is essential for success of resuscitation in the delivery room. In this article, we will briefly review transitional circulation focusing on altered hemodynamics of the complex congenital heart diseases and then discuss the process of preparing for these high-risk deliveries. Finally, we will review the pathophysiology resulting from the cardiac structural anomaly with resultant altered fetal circulation and discuss delivery room management of specific critical congenital heart diseases.

1. Introduction to the hemodynamic effects of critical congenital heart defects at birth

1.1. Fetal and transitional circulation

Knowledge of normal fetal and transitional circulations is essential for understanding the effect of congenital heart disease (CHD) and the associated altered blood flow in the fetus and the newborn. This in turn allows for anticipating the symptomatology and helps in management of these newborns in the delivery room (DR). We will briefly describe the normal fetal and transitional circulations as they have been described in detail elsewhere in this issue of Seminars. The most oxygenated blood coming from the umbilical vein first enters the portal venous system with about 50% of blood bypassing the liver via the ductus venosus flowing medially into the upper portion of inferior vena cava (IVC) [1,2]. This stream of blood flow is directed toward the foramen ovale by the Eustachian valve. In contrast, the poorly oxygenated blood flow from the lower part of the body flows along the lateral portion of IVC and is, in addition to superior vena cava (SVC) flow, directed toward the tricuspid valve. The most oxygenated blood, therefore, enters the left side of the heart and supplies the myocardium and brain. The right ventricle receives most of the systemic venous return; however, about 70–80% of the right ventricular output bypasses the high resistance pulmonary vascular bed via the ductus arteriosus to enter the descending aorta [2,3]. Therefore, both ventricles contribute to systemic blood flow with the right ventricle being the dominant ventricle and contributing about 55–60% of the combined cardiac output. At birth, there is a drop in pulmonary vascular resistance secondary to lung aeration and higher oxygen exposure, an increase in systemic vascular resistance secondary to removal of the low resistance placental circulation, and blood flow starts transitioning to a mature type of circulation. These changes result in a reduction or cessation of ductus venosus flow, reversal of flow through the ductus arteriosus and functional closure of the foramen ovale with no to minimal left-to-right flow.

In cases of CHD, the above described fetal circulation is altered and depending on the structural defect this alteration can be minimal and/or with no observable adverse effect on fetal growth and well-being, or it can severely impact the fetus and result in fetal demise. The changes in blood flow are specific to each CHD and the severity of the defect. Any defect resulting in either increased or decreased flow has both upstream and downstream effects. In addition to affecting the oxygen content of blood and the amount of blood supply to a vascular bed (lungs, brain, other organs), this altered blood flow leads to changes in

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Abbreviations

ACOG	American College of Obstetricians and Gynecologists
ASD	atrial septal defect
BAS	balloon atrial septostomy
CHB	complete heart block
DCC	delayed cord clamping
DR	delivery room
D-TGA	dextro-transposition of the great arteries
ECMO	extracorporeal membrane oxygenation
EXIT	ex utero intrapartum treatment
HLHS	hypoplastic left heart syndrome
ICU	intensive care unit
LOC	level of care
MOD	mode of delivery
PFO	Patent foramen ovale
PGE	prostaglandin E1
PR	pulmonary regurgitation
RAS	restrictive atrial septum
RV	right ventricle
TAPVR	total anomalous pulmonary venous return
TR	tricuspid regurgitation
TOF	tetralogy of Fallot
UVC	umbilical venous catheter
VSD	ventricular septal defect

growth of the heart chambers and vessels with further impact on hemodynamics. For example, in hypoplastic left heart syndrome (HLHS), hypoplasia of the aortic and/or mitral valve decreases forward flow through the left heart resulting in left ventricular hypoplasia and dysfunction as a result of coronary ischemia and endocardial fibroelastosis. The result is decreased LV compliance with increased ventricular filling pressure that in turn increases the left atrial pressure which reduces right-to-left shunt at the patent foramen ovale (PFO). In severe cases, the PFO shunt reverses (becoming left-to-right) leading to maldevelopment of the foramen. The reduction or cessation of blood flow through the aortic valve leads to hypoplasia of the ascending aorta and the aortic arch with brain oxygenation being compromised due to retrograde supply of less saturated blood from the patent ductus arteriosus (PDA).

The alteration of blood flow associated with CHD becomes a bigger challenge after birth. In addition, the normal increase in metabolism and oxygen consumption (breathing, thermoregulation, etc) after birth potentiate the effects of low oxygen saturation and blood flow in neonates that may be present in CHD. The timing and degree of cardiorespiratory compromise depends on the type and severity of the defect. For example, in HLHS, the low or absent flow through the aortic valve means that ductal patency must be maintained to ensure adequate systemic blood flow. More importantly, the already elevated left atrial pressure is further increased by the natural postnatal increase in pulmonary blood flow. This in turn can result in pulmonary congestion, respiratory distress and need for respiratory support. The severity of presentation in the DR in large part depends on the PFO flow. The more restrictive the PFO, the more severe the presentation will be at birth. This example highlights the importance of detailed assessment of the heart and fetal circulation for successful planning of delivery.

1.2. Definition of critical congenital heart disease

Complex forms of CHD often require early and/or emergent medical, surgical, or catheterization-based interventions in the first days to weeks of postnatal life. CHD lesions with inadequate aortic or pulmonary outflow can usually be stabilized in the neonatal period with medical therapy, using prostaglandin E1 (PGE) to maintain ductal patency, prior to cardiac intervention. However, critical forms of CHD have an additional element of instability during the perinatal transition period and often require emergent cardiac intervention in the first hours after delivery for stabilization and survival. These include lesions such as obstructed total anomalous pulmonary venous return (TAPVR) and HLHS with restrictive atrial septum (RAS) which lack adequate pulmonary egress, D-transposition of the great arteries (D-TGA) with RAS that limits intra-cardiac mixing, severe Ebstein anomaly and tetralogy of Fallot (TOF) absent pulmonary valve which are associated with airway anomalies that compromise the caregivers' ability to ventilate, and tachyarrhythmias or congenital complete heart block that result in inadequate cardiac output due to severe fetal tachycardia or bradycardia respectively. Most of these critical forms of CHD can be diagnosed with fetal echocardiography, which then allows for careful planning of maternal care to optimize the delivery and provide targeted postnatal care [4]. Furthermore, prenatal diagnosis can decrease perinatal morbidity and improve stabilization of patients prior to cardiac surgery [5,6]. Critical CHD diagnoses can be triaged using a combination of anatomic and physiologic fetal echocardiography findings to assign the appropriate risk level predicted postnatally [4,6,7]. This allows both the maternal and neonatal care providers the opportunity to carefully plan the perinatal care in order to optimize the delivery and provide targeted postnatal care.

1.3. Preparation for resuscitation of neonates with critical CHD

As preparation is made for resuscitation of a neonate with critical CHD, a careful review of the prenatal findings including fetal echocardiogram is crucial. A clear communication among the neonatologist, fetal cardiologist and the delivering obstetrician is paramount for the success of resuscitation. Categorizing patients into severity groups (see below) and understanding the severity of lesion are helpful in anticipating the interventions needed in the DR. Decisions regarding the use of delayed cord clamping should be made ahead of time and reviewed before delivery with the obstetrician.

The team should be assembled far in advance and briefed on the details of the case, the anticipated clinical status of the newborn, and any interventions that might be needed. Each team member should have a clear instruction on his/her role and understand how the role might change depending on the scenario encountered. All critical CHD deliveries should be attended by a neonatologist. As these patients often require respiratory support and intubation, a respiratory therapist should also be in attendance. In addition, at least 2 nurses are needed to assist with stabilization including emergency vascular access and chest compression. Other specialists may also be needed depending on the case. Transport team should be ready and on site for the delivery in the highest risk cases, those requiring emergent neonatal cardiac intervention, in order to facilitate immediate transfer to cardiac care and minimize time to intervention.

Although all supplies and equipment needed for a full resuscitation should be available for every delivery, in cases of critical CHD, additional steps need to be taken. An umbilical venous catheterization (UVC) insertion kit with the line flushed and ready for insertion and normal saline syringes for a total of 20–30 ml/kg bolus should be prepared in advance. Depending on the case, thoracentesis and pericardiocentesis set-ups, and prefilled epinephrine syringes should also be available prior to the delivery.

1.4. Perinatal management strategies to optimize postnatal transition

Active prenatal planning and perinatal management for neonates with CHD allow for a well-coordinated transition from fetal life to postnatal care, minimization of mortality and morbidity, and a stable pre-operative clinical status. Perinatal management action plans for critical CHD are now utilized by many centers across the United States and Europe using similar risk stratifying schemes with recommended care plans [6–9]. These classification systems are based on regional practice patterns and designed to identify patients that require specialized treatment in the DR and cardiac intervention in the first hours after delivery [10,11]. Cardiovascular disease severity scales are based on the anatomic severity of CHD, need for postnatal intervention, complexity of intervention and overall prognosis. The level of care (LOC) is typically assigned first by the cardiologist, according to the CHD diagnosis, and is then reviewed and agreed upon by the entire maternal fetal medicine team. Each LOC is linked with a specific coordinated action plan and detailed perinatal recommendations for delivery and DR management such as need for PGE, transport, and intervention. Risk stratification systems are designed for multiple levels of CHD severity and are used to select the appropriate medical center for delivery, mode of delivery (MOD), level of perinatology and neonatology services available, and capability for immediate access to cardiology and cardiothoracic surgery care. These risk stratification and LOC management plans for prenatally diagnosed CHD are highly accurate at predicting the postnatal care required and need for emergent intervention at birth [8]. These classification strategies have been highly reproducible with the exception of D-TGA due to the difficulty determining the risk for postnatal atrial level restriction. At our institution we developed a similar method of risk stratification of prenatally diagnosed cases of CHD that require emergent neonatal cardiac intervention, incorporating a four tier classification system, which we have termed “Emergent Neonatal Cardiac Intervention” (ENCI) risk categories (Table 1) [6]. A recent evaluation of this system at our institution showed an overall predictive ability of 89% with high adherence to recommendations, but not in all areas (unpublished data). This review led us to make additional improvements in LOC plans including standardizing communications, better prenatal coordination of the transport team and the addition of prenatal consenting for transport/procedures. Here is a review of the ENCI Risk Categories:

1.4.1. Level 1 (low risk)

CHD that does not cause hemodynamic instability and is not expected to require specialized care or intervention in the newborn period. Mothers can deliver at a hospital capable of providing care for babies with mild forms of CHD. MOD is not an issue and no special DR care is anticipated. Examples: atrial septal defect (ASD), ventricular septal defect (VSD), and mild valve abnormalities.

1.4.2. Level 2 (intermediate risk)

CHD with potential for hemodynamic instability and possible need for postnatal evaluation by subspecialists, but low risk for neonatal intervention. Mothers should deliver at a facility with access to neonatology and subspecialty consultation as needed. Delivery should occur in a facility with a Level III neonatal intensive care unit, in close proximity to a pediatric heart center. MOD is usually not an issue but must take into account any evidence of congestive heart failure or hydrops. Examples include complete atrioventricular septal defect, aortic arch obstruction, moderate valve abnormality and TOF with mild to moderate level of pulmonary stenosis.

1.4.3. Level 3 (moderate risk)

CHD that requires neonatal intervention in the first days to weeks after delivery, which includes all ductal dependent lesions. These deliveries should be highly coordinated and occur at or nearby tertiary care centers with a high level of neonatal and cardiac expertise. If early intervention is likely or there is increased risk for high acuity at birth, delivery by induction or scheduled C-section should be considered to provide a window of anticipated delivery. MOD must also take into account if there is any evidence of congestive heart failure or hydrops. Cardiac intensive care unit (ICU), cardiology, and cardiothoracic surgery should be notified well in advance of the delivery. Transport team should be notified and on standby, to expedite the transfer. Examples include D-TGA with VSD, HLHS without RAS, severe aortic or pulmonary valve abnormalities (including single ventricles), unobstructed TAPVR, TOF absent pulmonary valve without lobar emphysema, Ebstein anomaly without hydrops and complete heart block (CHB) with normal heart function and adequate HR (≥55 beats per minute).

1.4.4. Level 4 (high risk)

CHD requiring immediate or emergent intervention, within hours after birth, and in whom severe instability is anticipated. The perinatal care should be highly coordinated in order for all resources to be available at the time of birth. Mothers should deliver via scheduled C-section to minimize time to treatment with the necessary subspecialists on standby to care for the newborn. Ideally the delivery could occur in a highly specialized labor and delivery unit in a children's hospital for immediate intervention [8]. If transfer is needed the transport team should be on standby and present at the delivery institution. The baby must be adequately stabilized and monitored for transport, but performance of procedures in the DR must be balanced with the need to get the baby to intervention with minimal delay. Cardiac ICU, cardiology, and cardiothoracic surgery should be notified again immediately upon confirmation of birth. The operating room and/or cardiac catheterization laboratory should be on standby.

Examples include obstructed TAPVR, HLHS with RAS, D-TGA with RAS, TOF absent pulmonary valve with lobar emphysema, severe Ebstein anomaly with hydrops or uncontrolled arrhythmia and unstable

Table 1
Emergent neonatal cardiac intervention (ENCI) classification system.

ENCI Risk Level	Emergent Neonatal Cardiac Intervention	PGE Dependent	Mode of Delivery an Issue	NICU Acuity Level	Neonatologist present in DR	Critical Care Transport Needed	Cardiology, CT Surgery, CTICU, OR/Cath lab on Standby	Examples of CHD
I Low Risk	No	No	No	Low	No	No	No	ASD, VSD, mild PS
II Intermediate Risk	No	No	No	Mid	Possibly	Possibly	No	CAVC, TOF/PS, Truncus Arteriosus
III Moderate Risk	Possibly	Likely	Possibly	High	Yes	Yes	Possibly	HLHS, TOF/PA, PA/IVS
IV High Risk	Likely	Likely	Yes	High	Yes	Yes	Yes	D-TGA/RAS, HLHS/RAS, obstructed TAPVR

ASD, Atrial Septal Defect; CAVC, complete atrioventricular canal defect; Cath, catheterization; CT, Cardiothoracic; CTICU, Cardiac Intensive Care Unit; DR, Delivery Room; D-TGA, D-transposition of the great arteries; HLHS, hypoplastic left heart syndrome; NICU, Neonatal Intensive Care Unit; OR, Operating room; PA/IVS, pulmonary atresia with intact ventricular septum; PGE, Prostaglandin E1; PS, pulmonary stenosis; RAS. restrictive atrial septum; TAPVR, Total Anomalous Pulmonary Venous Return; TOF, tetralogy of Fallot; VSD, Ventricular Septal Defect.

CHB with slow ventricular rate (< 55bpm), decreased heart function, or hydrops fetalis.

2. Overview of critical CHD requiring emergent intervention in the DR

Critical CHD lesions can be grouped into four categories, by (1) inadequate flow of oxygenated blood to the systemic circulation, D-TGA with RAS; (2) inadequate pulmonary venous egress, TAPVR and HLHS with RAS; (3) associated lung or airway anomaly that compromises oxygenation and ventilation, severe Ebstein anomaly and TOF absent pulmonary valve; and (4) inadequate cardiac output, severe fetal arrhythmias and depressed cardiac function either in isolation or in combination with CHD. Here we will present one hypothetical case scenario to highlight the recommended perinatal care plan and DR management from each of the four categories of critical CHD (Table 2).

2.1. D-transposition of the great arteries with restrictive atrial septum

D-TGA is the most common cyanotic CHD in the neonatal period. Unlike cyanotic CHD with decreased pulmonary blood flow, neonates with D-TGA often present with severe cyanosis within minutes of birth. Neonates with D-TGA have pulmonary and systemic circulations in parallel rather than in series. Thus, to survive they must have adequate sites for mixing of blood between the two circulations to achieve adequate systemic oxygen delivery. While the presence of an associated VSD and PDA may allow for some mixing, these alone may be inadequate to provide effective oxygenated blood flow to the body. The most reliable strategy to achieve adequate systemic oxygen delivery is to establish an atrial level shunt, which often requires urgent balloon atrial septostomy (BAS), also known as the Rashkind procedure, within the first few hours of life. A balloon-tipped catheter is advanced from the femoral or umbilical vein through the IVC and right atrium, across the foramen ovale and into the left atrium where the balloon is inflated and rapidly pulled back across the atrial septum. By tearing across the

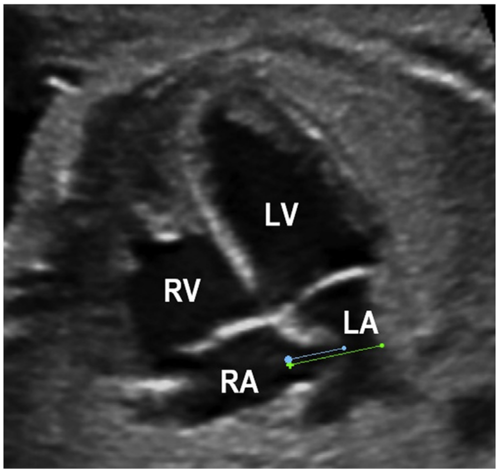

Fig. 1. Fetal echocardiogram four chamber view of D-Transposition of the Great Arteries case at 26 5/7 weeks' gestation demonstrating features of a restrictive atrial septum including hypermobile atrial septum primum with increased bowing into the left atrium (LA) with an atrial excursion ratio of 60% (blue line represents deviation of the septum primum by 5.2 mm, green line represents left atrial length of 8.7 mm). *RA, right atrium. RV, right ventricle. LV, left ventricle.*

Table 2
Delivery Room Management recommendations for ENCI Level 4 Cardiac Lesions.

Cardiac Lesion	DR Preparation	DR Resuscitation
D-TGA with restrictive/intact atrial septum	PGE available IV and UV catheter setup Inhaled nitric oxide if ductal flow abnormal Notify cardiology, cath lab	Initiate PGE via umbilical or peripheral line Intubation, mechanical ventilation (SPO_2 goal 75–85%) Consider inhaled nitric oxide if ductal flow abnormal Immediate transfer to cath lab for balloon atrial septostomy
HLHS with restrictive/intact atrial septum	PGE available IV and UV catheter setup Notify cardiology, cath lab and/or CT surgery	Initiate PGE via umbilical or peripheral line Intubation, mechanical ventilation (SPO_2 goal 75–85%) Immediate transfer to cath lab or OR for intervention to open atrial septum
Severe Ebstein anomaly	PGE available IV and UV catheter setup Antiarrhythmics if concern for tachyarrhythmia	Initiate PGE via umbilical or peripheral line Intubation, mechanical ventilation (SPO_2 goal > 90%) Consider 100% FiO_2 and inhaled nitric oxide to lower PVR Transfer to ICU when stabilized
TOF/APV	IV and UV catheter setup Notify cardiology	Consider 100% FiO_2 Prone positioning, try to avoid intubation if possible (risk of air trapping) Intubation and mechanical ventilation if necessary, consider higher PEEP (SPO_2 goal > 90%) Transfer to ICU when stabilized
Obstructed TAPVR	PGE available IV and UV catheter setup Notify cardiology, CT surgery	Initiate PGE via umbilical or peripheral line Intubation, mechanical ventilation (SPO_2 goal 75–85%) Consider ECMO Immediate transfer to OR for surgical repair
Tachyarrhythmias	Cardiac Monitor available for rhythm analysis IV and UV catheter setup Adenosine and antiarrhythmics available Defibrillator and neonatal pads available Notify cardiology	Cardioversion if unstable Rapid administration of adenosine via umbilical or peripheral line, if concern for SVT Transfer to cardiac center with electrophysiology when stable ECG, initiation of antiarrhythmic
CHB with HR < 55 bpm	Cardiac Monitor available for rhythm analysis IV and UV catheter setup Isoproterenol and/or epinephrine Pacer/defibrillator available (set to pacing mode) Temporary pacing pads Notify cardiology, CT surgery	Initiate chronotropic agent via umbilical or peripheral line, if HR < 55 bpm Transcutaneous pacing, if HR < 55 bpm Intubation, mechanical ventilation, if hydrops or myocardial dysfunction (SPO_2 goal > 90%) Immediate transfer to ICU, possibly to OR for temporary vs permanent pacing wires

CHB = complete heart block; CT = cardiothoracic; DR = delivery room; D-TGA = transposition of the great arteries; ECG = electrocardiogram; ECMO = extracorporeal membrane oxygenation; HLHS = hypoplastic left heart syndrome; HR = heart rate; ICU = intensive care unit; OR = operating room; PGE = prostaglandin E1; PVR = pulmonary vascular resistance; SPO_2 = arterial oxygen saturation; TAPVR = total anomalous pulmonary venous return; TOF/APV = tetralogy of Fallot absent pulmonary valve.

septum primum, a larger atrial communication is created which allows for adequate mixing of deoxygenated and oxygenated blood for stabilization.

Despite advances in prenatal diagnostic evaluation for prediction of the need for urgent BAS, there remains a high false negative predictive rate. Such predictive factors have included hypermobility of the septum primum, bowing of the septum primum into the left atrium by > 50% (Fig. 1), diminished mobility with an angle < 30° between the atrial septum and the septum primum [12–14]. Size and shunting pattern of the ductus arteriosus (reversed diastolic flow) and pulmonary vein peak systolic velocity > 41 cm/s have also been used with some degree of accuracy [13,15]. While delivery of fetuses with D-TGA is often classified as ENCI 3, when fetuses demonstrate any of the above findings concerning for postnatal atrial septal restriction, the delivery category elevates to ENCI 4. Given that the predictive value of these factors remains limited, one should consider all fetuses with D-TGA to be at risk for restriction of the atrial septum postnatally with associated hemodynamic instability.

2.2. Delivery room preparation

Due to the increased potential for requiring emergent neonatal intervention these mothers should deliver at a specialized labor and delivery unit equipped with facilities and staff capable of handling postnatal hemodynamic instability, with a plan for immediate postnatal evaluation by neonatology and cardiology. Given the possible need for an emergent BAS, these neonates should have immediate access to interventional cardiology that can perform a BAS procedure either at bedside with echocardiographic guidance or in a cardiac catheterization lab. If delivery cannot be performed at a children's hospital, transport should be arranged prior to delivery to ensure immediate transport to a hospital with access to cardiac care. If there is a high concern for intact or restrictive atrial septum on the prenatal echocardiogram, delivery by cesarean section is recommended.

Upon birth, cardiac ICU, interventional cardiology, and cardiothoracic surgery should be notified immediately. The latter should be on standby in case extracorporeal membrane oxygenation (ECMO) or surgical intervention is necessary. The cardiac catheterization laboratory and/or the operating room should be on standby for possible intervention.

2.3. Respiratory and cardiovascular support at birth

Initial DR management consists of assessment of respiratory effort, heart rate, circulation and color by the neonatology team. Target preductal oxygen saturation is in the range of 75%–85% after the first few minutes of transition and if supplemental oxygen is used, it should be adjusted to achieve this goal. Early elective intubation is recommended, as these patients have a high risk of respiratory decompensation. With intact atrial septum or severely RAS these patients show signs of cardiorespiratory failure in the DR shortly after birth. In rare circumstances there can be associated severe pulmonary hypertension which would necessitate iNO therapy and possible ECMO support [16]. Although opening the atrial septum by BAS is the main palliative treatment, administration of cardiac medications and judicious use of volume expanders via a low UVC made be necessary in the DR.

Soon after delivery and initial stabilization in the DR, venous access is obtained either by peripheral or standard umbilical venous line in order to administer PGE. This maintains ductal patency, thereby increasing pulmonary blood flow which in turn increases left to right shunting at the atrial level to improve systemic oxygen saturation. Position of the UVC should be verified by x-ray prior to transfer to avoid complications associated with administration of caustic medications. In addition, if PGE is infused via UVC, it is important to avoid having the catheter tip in portal venous system as the medication may not be effective.

The patient should be transferred immediately to a center with interventional cardiology available to perform a BAS and can be taken directly to the catheterization lab if preferred. An abbreviated transthoracic echocardiogram can be quickly performed to confirm the cardiac anatomy and to assess the patency of the foramen ovale and the ductus arteriosus. Emergent BAS can be performed either in the catheterization lab under fluoroscopy or at the bedside in the ICU via echo guidance.

2.4. Obstructed total anomalous pulmonary venous return

TAPVR accounts for only 0.5–2% of CHD, but continues to have one of the lowest rates of prenatal diagnosis and highest risks for mortality [17–19]. In TAPVR, pulmonary veins fail to return normally to the left atrium, but rather return to the right atrium via anomalous venous channels. There are four anatomical subtypes of TAPVR: 1) supracardiac (connects to the innominate vein or superior vena cava) 2) intracardiac (connects to the coronary sinus or right atrium) 3) infracardiac (connects to portal vein, hepatic vein, ductus venosus, or IVC) and 4) mixed type (connects at two or more of the above locations). Drainage is usually via a vertical vein, which is an embryologic venous remnant. Obstruction to pulmonary venous return can occur at multiple locations including at the vertical vein due to its length, at insertion sites of the draining vertical vein to the systemic venous system such as the portal or hepatic veins, and at areas of extrinsic compression such as between the left pulmonary artery and bronchus in the case of the supracardiac type. Obstructed TAPVR has important clinical consequences including acute postnatal severe congestion and pulmonary hypertension as well as the chronic pathological effects on lung development in utero [20]. Prenatal studies of predictors of TAPVR suggest the presence of a venous confluence, termed the twig sign, in the space between the atria and descending aorta (Fig. 2), abnormal spectral pulmonary venous waveforms, a smooth appearance of the posterior left atrial wall, and findings of an additional vessel representing a vertical vein can help increase the chances for a TAPVR diagnosis [21,22]. Vertical vein Doppler peak velocity > 0.74 m/s has been used to predict postnatal pulmonary venous obstruction [19].

Due to the nature of fetal circulation and the relatively small amount of pulmonary blood flow, TAPVR is well tolerated in utero. However, after birth, there is complete mixing of pulmonary and systemic blood in the right heart resulting in cyanosis as well as a lack of egress for pulmonary venous return resulting in severe pulmonary

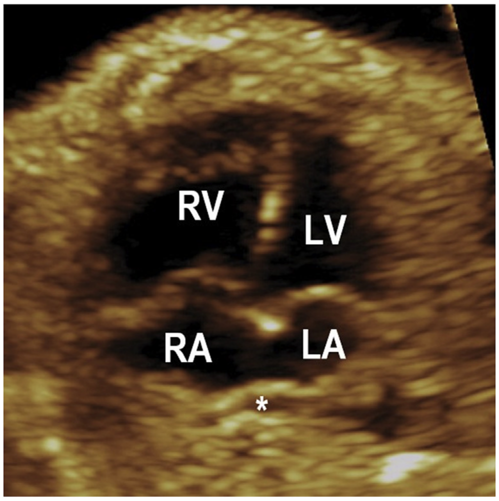

Fig. 2. Fetal echocardiogram of Total Anomalous Pulmonary Venous Return (TAPVR) case at 28 2/7 weeks' gestation demonstrating the "twig sign" with pulmonary veins seen draining into a confluence (*) behind the left atrium (LA) without a direct connection to the LA.

congestion and pulmonary hypertension presenting as severe respiratory distress.

2.5. Delivery room preparation

Due to the possibility of significant postnatal hemodynamic instability, a highly coordinated delivery plan should be in place to facilitate immediate stabilization and transfer for emergent TAPVR repair. In the case of TAPVR with concern for obstruction, scheduled C-section is recommended at most centers. The transport team should be on standby. The cardiothoracic surgery team should be prepared and operating room ready to receive the patient directly via transport as this remains one of the CHD lesions that can only be stabilized by emergent cardiac repair.

2.6. Respiratory and cardiovascular support at birth

Initial DR management consists of assessment of respiratory effort, heart rate, circulation and color by the neonatology team. The neonate may develop respiratory distress as a result of obstruction of the egress of pulmonary venous return and the development of pulmonary edema. The patient can also manifest with poor cardiac output and circulation, particularly if there is associated pulmonary hypertension. Hypoxemia and cyanosis is a common presentation due to mixing of the oxygenated pulmonary venous return and deoxygenated systemic venous return. Target preductal oxygen saturation is in the range of 75%–85%, however, in severe cases may be even lower due to a variety of factors including pulmonary edema and pulmonary hypertension. Supplemental oxygen should be adjusted to achieve this goal. Endotracheal intubation is recommended if there are signs of respiratory distress or significant hypoxemia.

After the initial stabilization in the DR, venous access is obtained either by peripheral or umbilical venous line. While PGE was previously thought to be unhelpful in TAPVR, recent literature suggests potential benefit in selected cases for two reasons: 1) to maintain patency of the ductus venosus in the case of infracardiac TAPVR as this is often the location of obstruction and 2) to maintain patency of the ductus arteriosus in the setting of pulmonary hypertension to allow adequate right to left flow across the PDA to maintain systemic blood flow [23,24].

The patient should be immediately transferred to a center with cardiothoracic surgery available. If the patient can be stabilized, a transthoracic echocardiogram can be performed in the ICU to confirm the prenatal diagnosis and characterize the degree of pulmonary venous obstruction. However, if the patient remains unstable, he or she should be taken directly to the operating room for surgical repair with intraoperative transesophageal echocardiography. If surgical repair is unable to be performed immediately, ECMO can be considered for stabilization prior to surgery.

2.7. Ebstein anomaly with severe tricuspid regurgitation

Ebstein anomaly is a rare congenital malformation characterized by apical displacement of the tricuspid valve that leads to tricuspid regurgitation (TR, Fig. 3). It occurs in 1–5 in 20,000 live births but when diagnosed in utero carries a high perinatal mortality rate as high as 45% [25]. In cases with severe TR, there is a large volume load on the right heart with associated right ventricular dysfunction. In the setting of decreased antegrade blood flow from the right ventricle (RV), pulmonary stenosis or atresia can develop, resulting in retrograde (left to right) ductus arteriosus flow. In severe cases, pulmonary regurgitation (PR) develops resulting in a circular shunt physiology. In this scenario, blood in the aorta flows retrograde through the ductus arteriosus into the pulmonary artery then back into the RV and into right atrium due to PR and TR. The blood in the right atrium then shunts across the foramen ovale from right to left atrium and flows again through the left heart and into the aorta thus completing the circle; this results in a steal of systemic cardiac output. As a result of elevated right atrial and systemic venous pressures due to TR, hydrops fetalis may develop. The combination of hydrops and low cardiac output leads to poor end organ perfusion and acidosis and ultimately leading to fetal demise. A large multicenter cohort study found the following to be predictive of perinatal mortality: gestational age < 32 weeks at diagnosis, larger tricuspid valve annulus z-score, presence of PR and pericardial effusion [25]. Outside of cardiac involvement, cardiomegaly can have a negative impact on lung development and patients are at risk for pulmonary hypoplasia.

Because this disease is progressive throughout gestation [26], routine surveillance should be performed to monitor for signs of hemodynamic compromise that would warrant earlier delivery. Premature delivery of neonates with heart disease has been associated with worse outcomes [27], so timing of delivery should be determined based on thoughtful discussion in the scenario of evolving fetal compromise. Fetuses with severe Ebstein anomaly often have difficulty transitioning to neonatal circulation due to inadequate pulmonary blood flow and lung hypoplasia leading to cyanosis and low systemic blood flow.

2.8. Delivery room preparation

With the potential for significant respiratory and hemodynamic compromise, a highly coordinated delivery plan should be in place with the neonatologist present in the DR for immediate postnatal assessment and medical management. Transport team should be on standby for rapid transfer to a center with cardiology and cardiothoracic surgery services. The cardiothoracic surgery team should be made aware of the patient's delivery, as significant postnatal instability may necessitate ECMO support [28].

In addition to poor cardiac output as highlighted above, patients with Ebstein anomaly have a higher incidence of supraventricular tachyarrhythmias (at least 15%) and ventricular pre-excitation (10–29%) due to the abnormal development of the tricuspid valve [29]. Thus, antiarrhythmic medications such as adenosine should be prepared prior to delivery, especially if there is a known fetal arrhythmia.

2.9. Respiratory and cardiovascular support at birth

In severe Ebstein anomaly, initial assessment of respiratory status may reveal significant respiratory distress and cyanosis due to lung hypoplasia and thus these patients often require intubation in the DR. Regarding ventilator strategy, the minimum needed mean airway pressure to avoid atelectasis should be used to avoid hyperinflation [30]. If there is pulmonary atresia or regurgitation, the goal of

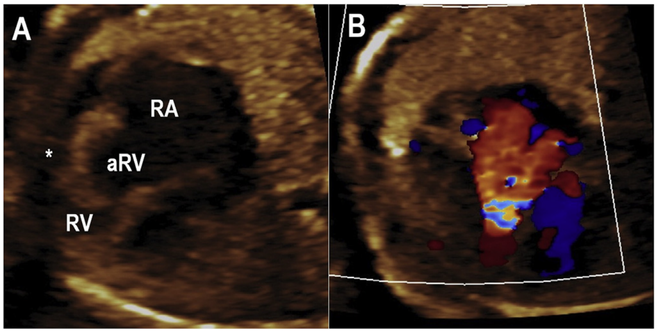

Fig. 3. Panel A: Fetal echocardiogram of Ebstein anomaly at 22 4/7 weeks gestational age with severe inferior displacement of the tricuspid valve into the right ventricle (RV) resulting in a large portion of atrialized right ventricle (aRV) and dilated right atrium (RA). A small pericardial effusion (*) is also noted. Panel B: the severe displacement of the tricuspid valve is associated with severe tricuspid regurgitation that has resulted in RA dilation.

management will be to lower the pulmonary vascular resistance to decrease the afterload that the struggling RV is facing. This can be accomplished with oxygen, inhaled nitric oxide, and correction of acidosis. When pulmonary artery pressure is lower than RV pressure, the pulmonary valve may open to allow antegrade pulmonary blood flow.

Intravenous access, preferably UVC, should be placed immediately given the potential need for medications for arrhythmias or inotropes in the case of low cardiac output. Target arterial oxygen saturations are 75–85% but profound hypoxemia may occur. PGE should be started to ensure pulmonary blood flow via PDA in cases of severe RV dysfunction. Initial management is mostly medical but cardiothoracic surgical team should be on standby in case ECMO is required.

2.10. Complete heart block

Immune-mediated CHB is seen in fetuses of mothers who are positive for SSA/SSB antibodies. Fetuses usually have structurally normal hearts and the mechanism of CHB is immune-mediated inflammation and fibrosis of the atrioventricular node (Fig. 4). Approximately 2–4% of pregnant mothers with positive antibodies develop fetal CHB, and if a prior sibling had CHB, the risk increases to 16% [31]. Many prophylactic treatments have been trialed including intravenous immunoglobulin, plasmapheresis and dexamethasone without noted decreases in the rate of fetal CHB; hydroxychloroquine is currently being studied [32,33]. While CHB is irreversible once it develops, treatment of second-degree heart block has been reported to be successful in preventing progression to CHB [34]. Unfortunately, the evolution of normal sinus rhythm into CHB is so rapid (usually < 24 h) that these fetuses are usually not identified in time to receive appropriate therapies [35]. Once CHB has developed, fetal management has relied on a weak evidence base for treatment with dexamethasone or intravenous immunoglobulin to prevent progression of immune-mediated effects on the heart such as atrioventricular valve insufficiency, ventricular dysfunction, endocardial fibroelastosis, and hydrops [36,37]. Sympathomimetics such as terbutaline or salbutamol have been used by some to increase the heart rate when average fetal heart rates fall below 55 bpm which predicts a poor prognosis [38]. After birth, the patient's heart rates, clinical status, ECG and ECHO findings need to be evaluated to determine need for neonatal support and timing of permanent pacemaker implantation.

2.11. Delivery room preparation

Due to inability to use heart rate as a measure of fetal well-being, an elective C-section is recommended at 39 weeks if the fetus is otherwise stable. If there is progression of cardiac disease involving the development of worsening heart failure or hydrops, an earlier delivery should be considered. A delivery plan should be made to include neonatology and cardiology teams. Isoproterenol, epinephrine and dopamine should be prepared and ready if needed for extremely low heart rates with evidence of low cardiac output. The transport team should be on standby and the cardiothoracic surgery team and cardiology notified in the cases that may require emergency temporary pacing followed by early pacemaker implantation.

If the neonate is unable to undergo pacemaker placement immediately after birth, temporary pacing strategies can be initially utilized to stabilize prior to surgery. Transcutaneous and transvenous pacing are two common strategies, both of which have advantages and disadvantages. Transcutaneous pacing involves application of pacing pads, which can be difficult in a newborn due to the presence of vernix and may result in thermal injury. Furthermore, sedation of the newborn is often required and elective intubation is recommended due to complications with apnea from transcutaneous pacing. Transvenous pacing is performed by placing a pacing catheter directly into the right ventricular apex through a femoral, internal jugular, or umbilical venous approach [39]. While more often utilized in older children, transvenous pacing in the newborn can be challenging due to difficulty obtaining venous access in situations with low cardiac output as well as the additional complication risks of venous thrombosis and infection [40]. In one case of anticipated severe fetal bradycardia, an ex utero intrapartum treatment (EXIT) procedure was reported in which a uterine incision was performed and a temporary epicardial pacing wire was sutured directly onto the right ventricle through a subxiphoid approach, before the umbilical cord was clamped and the patient was delivered [37]. This allowed for immediate ventricular pacing at birth and resulted in a more stable completion of delivery and postnatal course before undergoing permanent pacemaker placement. While the above strategies are options in an emergent scenario, ultimately, surgical placement of an epicardial pacemaker lead is the definitive treatment.

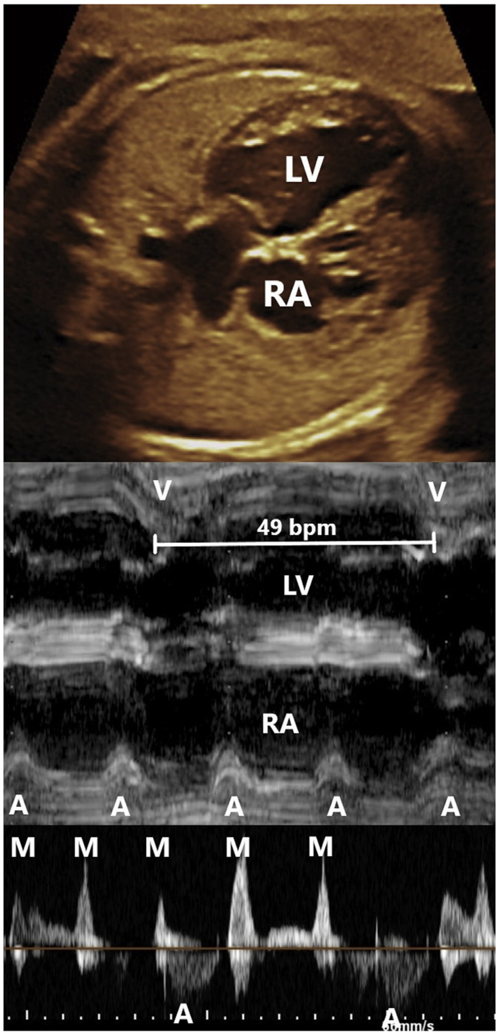

Fig. 4. Fetal echocardiogram of a fetus at 24 2/7 weeks' gestation with complete heart block secondary to maternal SS-A antibodies shows a severe cardiomegaly with a CTA ratio of 0.52 and a small pericardial effusion without evidence of hydrops (upper panel). There was also moderate mitral and tricuspid regurgitation (not shown). In the middle panel, a fetal M-mode through the left ventricle (LV) and right atrium (RA) shows complete dissociation of atrial (A) and ventricular (V) contraction with a ventricular rate of 49 bpm. In the lower panel, a pulse wave Doppler interrogation shows dissociation of the mitral valve (M) inflow and aortic (A) outflow.

2.12. Respiratory and cardiovascular support at birth

Initial assessment includes evaluation of respiratory effort, heart rate, circulation and color. Due to normal cardiac anatomy, target saturations are within normal range. If heart rate is above 55bpm without other signs of respiratory or cardiovascular compromise, elective intubation is not recommended. If, however, the heart rates are below 50 bpm with history of decreased cardiac function or fetal hydrops, elective intubation and placement of umbilical catheters is recommended. The patient should be transferred immediately to a facility with cardiology and cardiothoracic surgery available. Isoproterenol can be initiated if heart rates remain < 55 bpm; additionally, epinephrine may be considered for both chronotropic and inotropic support. PGE is not recommended unless there is another associated congenital defect that is ductal dependent. If not responsive to medications, temporary pacing can be performed at bedside, but the cardiothoracic surgery team should be notified for impending need for surgical pacemaker placement. Once stabilized, electrocardiogram and echocardiogram should be performed. The patient should remain on telemetry for close observation of heart rate and rhythm.

3. Other considerations

3.1. Fetal intervention improving DR management

Fetal intervention has the potential to alter the CHD disease state prenatally and result in a lessening of the acuity at neonatal presentation of CHD and improving the pre-operative clinical condition. Although appropriately designed, controlled trials have not been performed yet and might not even be feasible, findings of large case series suggest that balloon valvuloplasty of the aortic valve in cases of critical aortic stenosis may prevent progression to HLHS resulting in a more stable biventricular circulation at birth [41,42]. These patients may go from being ductal dependent at birth to not requiring a PGE infusion and possibly avoiding neonatal surgery. HLHS with RAS can also be stabilized with prenatal/fetal intervention by the creation of an atrial communication using either balloon septostomy or inter-atrial stent placement in the fetus [43]. This has the potential to improve the physiology, stabilize the newborn, and avoid the need for emergent surgical or catheter based septostomy in the first hours after delivery. Medical fetal therapy with digoxin for fetal congestive heart failure, anti-arrhythmia drugs for fetal supraventricular tachycardia and fetal transfusion all have the potential to mitigate fetal congestive heart failure and reverse fetal hydrops. Therefore, these treatments can improve fetal status prior to delivery and result in better neonatal outcomes [44]. Emerging therapies such as implantable fetal pacemakers for congenital CHB may help carry a pregnancy to term or near term and reverse fetal hydrops, resulting in a better clinical status at birth prior to permanent pacemaker implantation [45,46]. While many of these fetal cardiac interventions are novel with results reported in relatively small numbers, this remains an active area of research with both US and international collaborations coming together to study their potential [42].

3.2. Delayed cord clamping

A 30–60 s delay in umbilical cord clamping in a vigorous term and preterm infants is currently recommended by the American College of Obstetricians and Gynecologists (ACOG) and endorsed by the American Academy of Pediatrics [47]. On the other hand, ACOG recommends immediate cord clamping, or individualized approach when there is a need for immediate neonatal resuscitation. There are significant benefits to delayed cord clamping (DCC) including increased hematocrit and iron stores as a result of placental transfusion. In the term neonate, about 16 and 23 ml/kg of blood is transfused from the placenta to the neonate with a 1- and 3-min DCC, respectively [48]. While not a consistent finding, the benefits of DCC may be greater among preterm infants including more stable hemodynamic status during the transitional period [49–52]. The onset of breathing before cord clamping promotes earlier establishment of pulmonary blood flow and increases left ventricular preload for a more gradual separation from the low resistance placental circulation which may facilitate better adaptation of the left ventricle to the postnatal increase in afterload [53]. While the above mechanisms may play a role in the observed improvement in transition, the findings of similar benefits with cord milking suggests that placental transfusion is the key factor [54–56].

There is a theoretical benefit to DCC among infants with CHD, especially those with cyanotic lesions. The increased oxygen carrying capacity and higher blood volume would improve tissue oxygenation when oxygen saturation and blood flow are low. On the other hand, increased viscosity associated with higher hematocrit and volume overload could be problematic in cases of depressed heart function. In addition, the need for prompt resuscitation in critical CHD makes DCC in such circumstances more controversial. An Italian task force recently recommended DCC for newborns with CHD taking an individualized approach to guide cord clamping in severe CHD cases (i.e. critical CHD) based on expert opinion and a small pilot RCT trial [57,58]. This trial compared delayed versus early cord clamping in newborns > 37 weeks' gestation with CHD (defined as heart lesions other than single ventricle physiology and likely to require surgery or cardiac catheterization within the first 30 days) [58]. They found DCC to be safe and feasible in this high-risk population. In addition, the DCC group had higher initial hematocrit and overall required less blood transfusion. Further studies are needed to confirm the safety and investigate short- and long-term implications of DDC in newborns with CHD.

4. Conclusions

Neonates with critical CHD are at increased risk of mortality and morbidity due to their underlying heart condition and the hemodynamic changes that occur immediately postnatal in the DR. Improvements in ultrasound scanning technology and enhanced screening guidelines continue to increase prenatal detection of CHD, identify reliable fetal echocardiographic markers for predicting emergent neonatal intervention and improve perinatal strategies for those newborns at greatest risk. Critical CHD requires a highly coordinated perinatal plan and DR management strategy for appropriate stabilization and immediate transition of care to the cardiac team. Once a diagnosis of critical CHD is made there should be a comprehensive care plan developed based on the anticipated postnatal acuity level and need for emergent intervention. Active perinatal strategies and DR protocols as well as close multidisciplinary collaboration hold the promise of improving the approach to complex CHD, but are still being refined. In the future, innovative fetal therapies may alter outcomes for some forms of critical CHD and allow for a less critical transition from fetal to postnatal life. However, until that is fully realized, the best opportunity to improve outcomes for our most critical CHD neonates is a well-developed and executed perinatal plan.

4.1. Learning points

1. While the altered fetal circulation associated with critical CHD is often well-tolerated in utero, the transition to neonatal circulation is complicated and these patients often require cardiorespiratory support in the delivery room.
2. Risk stratification and level of care management plans for prenatally diagnosed CHD are useful for predicting the postnatal care required and need for emergent intervention at birth.
3. Careful review of the prenatal findings including fetal echocardiogram and clear communication among the neonatologist, fetal cardiologist and the delivering obstetrician are crucial for successful resuscitation.

5. Research directions

1. Further refinement of prenatal prediction of need for delivery room intervention in critical CHD, especially for D-TGA.
2. Fetal intervention aiming at reducing the severity of CHD and mitigating the need for emergent intervention in the delivery room.

Declaration of competing interest

None of the authors had any conflict of interest.

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Delivery room emergencies due to birth injuries

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ABSTRACT

Delivery room emergencies due to birth injuries are serious, usually unexpected, and can be distressing situations that necessitate immediate action to reduce neonatal morbidity and prevent neonatal mortality. Birth injuries requiring immediate, urgent care in the delivery room are uncommon, hence knowledge of obstetric risk factors and prenatal conditions linked to birth injury is an important first step in the management of affected neonates. Furthermore, immediate recognition of injury and quick action upon delivery is essential in order to achieve the best possible outcomes. This chapter briefly reviews the known risk factors associated with birth injury, and then discusses the identification and management of specific injuries that may require immediate treatment in the delivery room, or hasty management within hours after birth.

1. Introduction

Birth injury is described as an impairment of a newborn's body function or structure secondary to an adverse, often unexpected event that occurred during labor, delivery, or both. While most birth injuries are nonintentional, some injuries are the result of efforts to rapidly deliver an infant in the setting of maternal compromise or fetal distress. The majority of birth injuries are not life-threatening, and most do not require interventions in the delivery room. For purposes of this review, the more common birth injuries, such as fractures and lacerations, will not be discussed due their generally benign nature.

Fortunately, the overall incidence of birth injuries has declined due to enhancements in prenatal diagnosis and improvements in obstetrical care. The estimated incidence of birth injury is approximately 2% for single vaginal deliveries from the cephalic position, and approximately 1.1% for cesarean deliveries [1,2]. As these numbers indicate, mode of delivery and fetal position (cephalic versus breech) are some of the factors that influence the risk of birth injury. Moczygemba et al. estimated an overall birth trauma rate of approximately 2.6% when analyzing U.S. data from the Nationwide Inpatient Sample of over eight million newborns born between 2004 and 2005 [3]. Risk factors associated with birth injury have been well defined, enabling the obstetrician to recognize the potential for injury and adjust maternal care in order to avoid trauma to the neonate (e.g. elective cesarean delivery). Likewise, based on the obstetric and peripartum history, the neonatal team is able to anticipate certain scenarios in which emergent interventions in the delivery room may be necessary. However, it is important to note that despite best efforts to anticipate trauma to the neonate, significant birth injury can occur in the setting of a low risk gravida, uncomplicated pregnancy, and/or normal labor course.

This chapter focuses on the diagnosis and treatment of certain birth injuries that require intervention soon after delivery in order to decrease neonatal morbidity and, in some instances, prevent neonatal death. Fortunately, neonatal death attributed to birth injury is rare, with a reported incidence of less than 2% [4]. Management of these neonates may require urgent attention in the delivery room or, if the birthing facility has a neonatal intensive care unit (NICU) in close proximity to the delivery room, the neonate can be expeditiously transferred to the NICU for care. For purposes of this chapter, birth injuries with the following characteristics are deemed emergencies and require immediate management: 1) injuries associated with acute blood loss and shock, 2) injuries that may result in respiratory insufficiency or failure, and 3) injuries that carry a risk of neurological or organ impairment.

2. Risk factors

Known risks for neonatal birth injury have been attributed to maternal factors, fetal factors, and to the use of instrumentation during delivery. Likewise, a combination of these risk factors further increases the likelihood of birth injury. When significant risk factors for birth injury are present, a team of skilled providers should be assembled and present at delivery to provide immediate care to the newborn.

2.1. Maternal factors

Maternal obesity, defined as a body mass index (BMI) greater than 30 kg/m^2, is considered one of the most commonly occurring risk factors seen in obstetric practice and is associated with an increased risk of birth injury [5,6]. The etiology of this increased risk is likely due to a higher incidence of gestational diabetes, increased use of instrumentation (section 2.3), shoulder dystocia (section 2.4), and

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increased incidence of large for gestational age (LGA) newborns in women who are obese. In analyzing outcomes from over 350,000 pregnancies, Jolly et al. reported that women with a BMI greater than 30 kg/m2 were more likely to deliver a newborn with excessive birth weight, have an instrumented delivery, and have a newborn that was admitted to the special care baby unit [7].

2.2. Fetal factors

Excessive fetal weight and abnormal presentation are associated with an increased risk of birth trauma. The term macrosomia is used to describe newborns with excessive birth weight and, although definitions vary in the literature, most experts define macrosomia as a birth weight of greater than 4000 to 4500 g. Studies show newborns with birth weights ≥4000–4500 g to be at increased risk for a variety of injuries related to birth trauma, including brachial plexus injury, phrenic nerve injury, fractures, soft tissue injuries, and abdominal injury. Nassar et al. reported a 7.7% risk of birth injury in a retrospective review of 231 newborns with birth weights > 4500 g [8]. When comparing newborns of birth weight ≥4000 g to newborns with birth weights of 3000–3999 g, Boutlet, et al., observed an increase risk of neonatal complications as the birth weight increased beyond 4000 g, with newborns of birth weight > 4500 g being at particular risk of morbidity and mortality [9]. Abnormal fetal lie, defined as fetal presentation other than cephalic, is also associated with an increased risk of birth trauma. Infants delivered via vaginal breech extraction are at particular risk for birth injury, and specific criteria have been established to minimize risk for women who desire a trial of vaginal breech delivery [10].

2.3. Use of instrumentation

Multiple publications have shown an increased incidence of birth injury with the use of forceps or vacuum assistance during delivery. Both forceps and vacuum delivery have an increased risk of birth injury when compared to non-operative vaginal delivery, or delivery by cesarean section, with or without labor [1,11]. Both forceps and vacuum extraction are recognized as acceptable for instrumented delivery [12], and each has been associated with specific types of birth injuries.

2.4. Shoulder dystocia

An obstetric emergency, shoulder dystocia is defined as a delivery that requires additional obstetric maneuvers to release the shoulders when gentle downward traction has failed to affect delivery [13]. Spong et al. generated an objective measure for shoulder dystocia, and proposed that a prolonged head-to-body delivery time of more than 60 s be included in the definition [14]. Shoulder dystocia is associated with both maternal and neonatal morbidity, and is often accompanied by other risk factors for birth injury, such as fetal macrosomia and instrumented delivery.

3. Resuscitation in the delivery room

Per international guidelines for neonatal resuscitation, every birth should be attended by at least one individual whose only responsibility is the care of the newborn. This individual is expected to be skilled in the initial steps of resuscitation: warm the neonate, clear secretions if copious and/or obstructing the airway, dry, stimulate, and initiate positive pressure ventilation if needed. Furthermore, every birthing facility should have additional personnel available who are skilled in all aspects of neonatal resuscitation, including endotracheal intubation, umbilical vein catheter placement, and the administration of medications, fluids, and blood products [15]. Volume expansion may be considered when blood loss is unknown or suspected based on exam findings such as pallor, weak pulse, poor perfusion, and if the infant's heart rate has not adequately responded to other resuscitative measures [16].

3.1. vol resuscitation

Volume resuscitation of the newborn in the delivery room is potentially life-saving and, fortunately, is a rare occurrence. In a large retrospective review of 37,972 liveborn infants, thirteen were treated with volume infusions in the delivery room and, of those thirteen, only three received volume for suspicion of hypovolemia [17]. Objective measures of newborn circulatory status in the delivery room are needed for assessing infants with suspected hypovolemic shock. Per the Neonatal Resuscitation Algorithm, assessment of heart rate is the mainstay by which to gauge the need for resuscitation, and to assess the newborn's response to resuscitative efforts [16]. Pulse oximetry during stabilization is traditionally used to monitor the newborn's heart rate however, electrocardiogram monitoring with the placement of three chest leads has been shown to provide more accurate heart rate values in a shorter period of time than pulse oximetry, and is less prone to movement artifact [18]. Non-invasive (cuff) blood pressures can be obtained during newborn stabilization, but these measurements have been shown to be inconsistent and may not be clinically useful as a means of assessing circulatory status. Invasive monitoring, such as placement of an arterial line, is not practical in the delivery room setting [19]. When birth history and the newborn's initial presentation suggest hypovolemic shock, volume resuscitation with whole blood or crystalloid solution (normal saline) should be urgently provided. Colloid infusions, such as albumin, are not advised as a treatment option during delivery room stabilizations [20]. Whole blood is preferred over normal saline because it provides volume, colloid, and oxygen carrying capacity, and urgent transfusion with uncrossmatched O-Rhesus-negative blood should be administered whenever available [20,21]. The recommended initial dose is 10–20 milliliters/kilogram, with repeat doses as needed based on the newborn's response.

4. Cranial injuries

Birth injuries sustained to the head may involve intracranial structures and/or extracranial structures. Some of these injuries are associated with significant morbidity and mortality, hence it is imperative to recognize them early and initiate treatment as soon as possible.

4.1. Intracranial hemorrhages (ICH)¶

Intracranial hemorrhages are described according to location and, in order of incidence, include: 1) subdural, 2) subarachnoid, 3) epidural, and 4) intraventricular. Not surprisingly, the incidence of all types of intracranial hemorrhage is reported to be five to ten times higher for neonates delivered by forceps or vacuum extraction [1]. In general, birth injuries due to intracranial hemorrhage do not require urgent intervention in the delivery room setting. However, affected newborns may become symptomatic within hours of delivery, requiring early recognition and intervention to avoid significant morbidity. Subdural hemorrhage (SDH) refers to bleeding between the dura mater and the arachnoid layer of the brain caused by rupture of the bridging veins, and is usually tentorial or interhemispheric in location (Fig. 1). The reported incidence varies widely, as SDH has been reported to be a common finding upon imaging of the newborn brain shortly after delivery with incidences as high as 26% [22] and 46% [23], for infants born via instrumented and non-instrumented deliveries. Subarachnoid hemorrhage, the second most common type of neonatal intracranial hemorrhage, is caused by rupture of bridging veins in the subarachnoid space or small leptomeningeal vessels. Epidural hemorrhage (EDH) occurs between the dura and inner table of the skull and is attributed to injury to the middle meningeal artery. Typically located in the parietotemporal region, epidural hemorrhage is often accompanied by

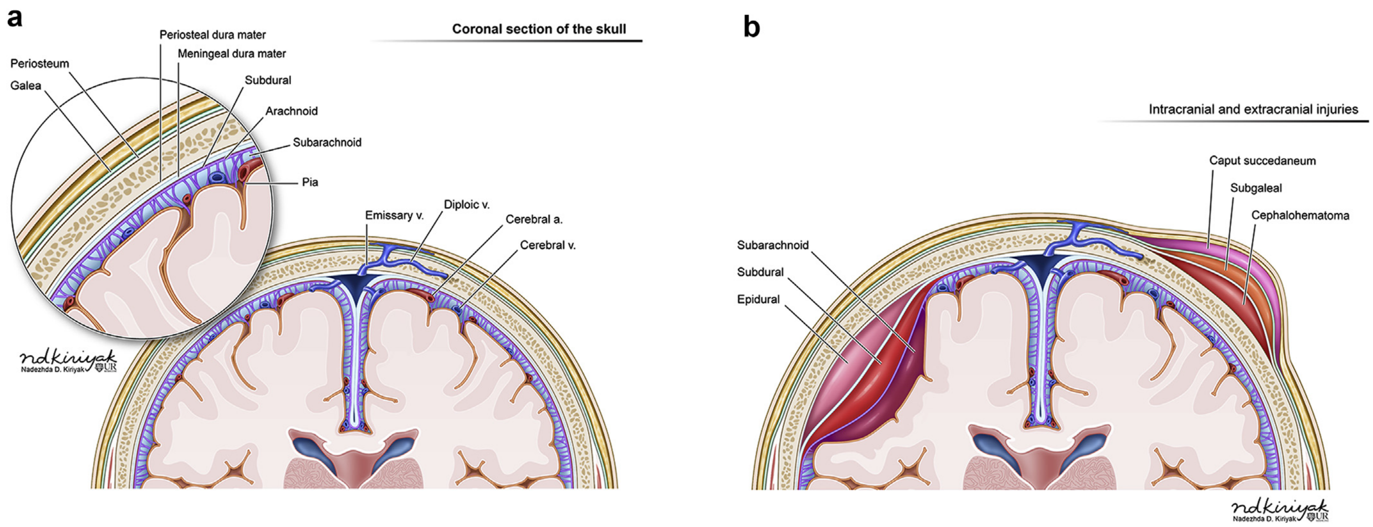

Fig. 1. A Coronal section of the skull. Used with permissions. B Intracranial and extracranial injuries. Used with permissions.

skull fracture which can enhance bleeding by shearing of the underlying blood vessels. Intraventricular hemorrhage (IVH) is most often associated with premature infants, with an increasing incidence as gestational age decreases. While uncommon, IVH has been reported in term infants, for which primary management rarely includes early intervention.

Management/Intervention: Newborns with ICH requiring urgent intervention usually exhibit symptoms within hours after delivery. However, because symptoms can be delayed, asymptomatic newborns with suspected ICH should be monitored closely after delivery in a nursery setting that allows frequent assessment of vital signs, serial physical exams, including serial measurement of frontal-occipital circumference (FOC), and ready access to diagnostic imaging. Symptoms associated with ICH include: apnea, seizures, respiratory depression, altered tone, decreased level of consciousness, and increased irritability [24]. These symptoms, particularly in the setting of vacuum or forceps delivery, require urgent imaging of the head. When performed by an experienced technician or radiologist, bedside ultrasound is a safe and rapid tool to assess the presence of intracranial hemorrhage, followed by definitive study with computed tomography (CT) or magnetic resonance imaging (MRI) [25]. While convenient and free of radiation exposure, images obtained via ultrasound are limited by the size of the fontanel, hence peripheral ICH can be missed, and epidural hemorrhage is rarely detected. CT has been described as the preferred method for rapid detection of ICH due to ease of access and shorter scan time [24]. To avoid significant morbidity, and mortality, neurosurgical intervention is sought in the setting of deteriorating neurological function with evidence of brain compression, or when symptoms and imaging are consistent with increased intracranial pressure. However, it is important to remember the flexibility of the newborn skull – owing to unfused sutures - and the presence of fontanels that serve as a “pop off” may compensate for the presence of increased intracranial pressure. For this reason, size or thickness of the bleed has also been used as a determinant for surgical intervention [26]. In an analysis by Pollina et al. of 41 newborns with cranial birth injuries, five infants (12%) required operative treatment, and two of the 41 infants died. Posterior fossa SDH, although uncommon, can be acutely life-threatening due to compression of the brainstem. In a retrospective analysis by Blauwblomme et al. of sixteen neonates with posterior fossa hematoma, nine neonates had evidence of brainstem dysfunction within the first 24 h of life, and eleven required surgical evacuation of the posterior fossa SDH [27]. EDH is more likely than SDH to present with signs of increased intracranial pressure in the first hours of life, likely due to the arterial etiology of the hemorrhage, particularly when accompanied by skull fracture. In his study of fifteen neonates with epidural hematomas, Heyman, et al. observed skull fractures in ten of the babies, with six of the ten fractures described as depressed. Seven neonates (46%) in this series were treated with craniotomy to evacuate the EDH, including all six babies with a depressed skull fracture [26].

4.2. *Extracranial injuries¶*

Extracranial injuries sustained as a result of birth trauma include: 1) caput succedaneum, 2) cephalohematoma, and 3) subgaleal hemorrhage (SGH). Of these, only SGH has been associated with significant morbidity and mortality. SGH is caused by traction on the scalp during delivery with subsequent shearing or severing of the emissary veins that lie in the space between the skull periosteum and epicranial aponeurosis (subgaleal space) [Fig. 1A and B]. SGH is associated with instrumented delivery, with vacuum assistance carrying a much higher risk of SGH than forceps. The incidence is estimated to be 4 per 10,000 non-instrumented deliveries, and as high as 64 per 10,000 vacuum-assisted deliveries [28,29]. Maternal nulliparity, Apgar score of less than 8 at five minutes, marks of vacuum cup over the sagittal suture, and marks of leading edge of the vacuum cup < 3 cm away from the anterior fontanel of the head have also been identified as risk specific factors for SGH [30]. Essentially a huge potential space, the subgaleal space extends from the orbital ridges anteriorly to the nape of the neck posteriorly and to the level of the ears laterally. Bleeding can be massive, allowing for sequestration of 20–40% of the newborn's blood volume, or more, into the subgaleal space [31]. The mortality rate for SGH is high due to the potential for hypovolemic shock and associated coagulopathy. Kilani and Wetmore report a mortality rate of 11.8% in their study of 34 newborns with SGH, all died from significant volume loss, coagulopathy, and shock [32]. In an analysis of data collected prospectively on 69 newborn with SGH, Gebremariam reported a 14% mortality rate [33]. A more recent analysis of 20 newborns diagnosed with SGH, eighteen of whom were delivered via vacuum assistance, reported a mortality rate of 15% [34]. Amar et al. reports the unusual presentation of severe extracranial cerebral compression in two newborns with massive SGH, in which one of the neonates did not survive [35].

Management/Intervention: Early recognition and intervention is imperative to decreasing morbidity, preventing mortality, and improving long term outcomes. In a prospective observational study of 71 infants for which active screening for SGH, and early, aggressive treatment was initiated, the reported mortality rate was 2.8% [30], much lower than other published reports. SGH should be suspected in

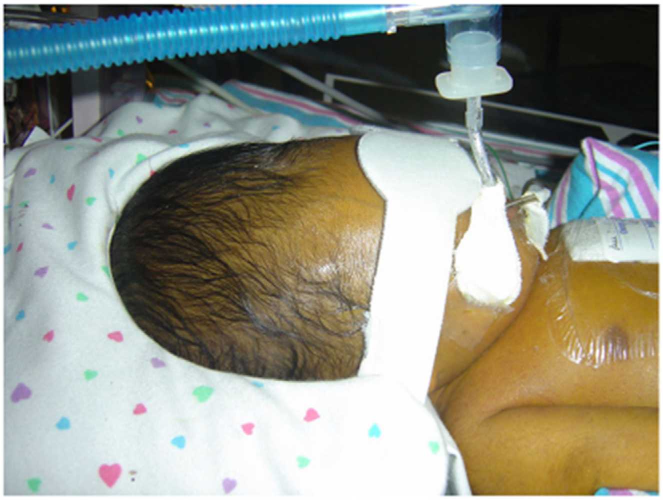

Fig. 2. Newborn with severe subgaleal bleed subsequent to vacuum delivery. Scalp is boggy and fluctuant to palpation. Photo courtesy of Gerardo Cabrera-Meza MD.

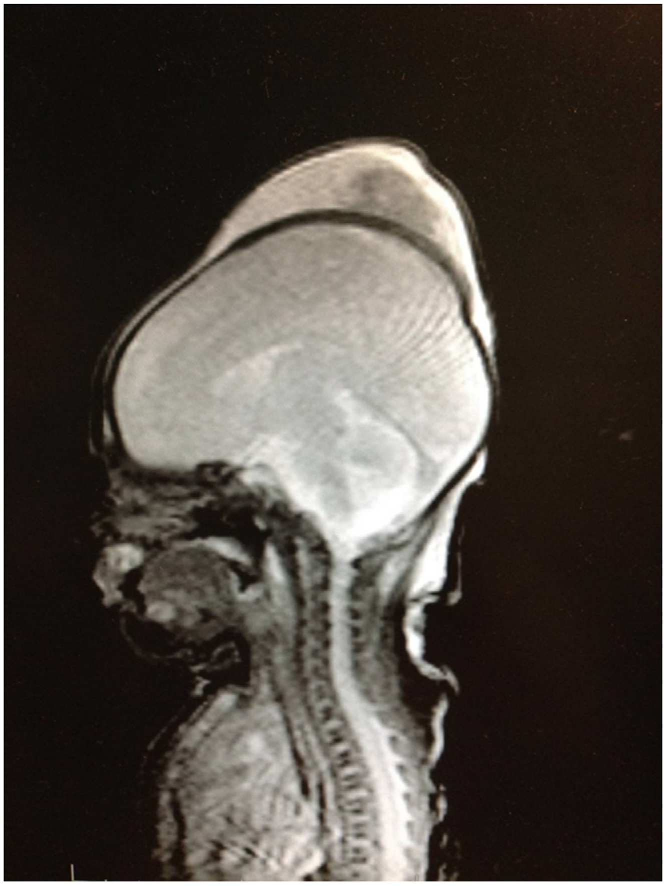

Fig. 3. Subgaleal bleed Image courtesy of Gerardo Cabrera-Meza MD.

any newborn presenting with fluctuant swelling of the head that crosses suture lines, particularly when delivery was complicated by the use of forceps or vacuum extractor (Figs. 2 and 3). While intervention in the delivery room is likely not needed, identification of newborns at risk for SGH should occur soon after delivery, and at risk infants should be admitted to a special care nursery for close monitoring. Monitoring of these infants must include: 1) continuous heart rate monitoring or frequent assessment of vital signs (every one to four hours), 2) serial measurements of FOC, as a one centimeter increase in FOC can represent 30–40 mL of blood loss into the subgaleal space [36], and 3) serial hematocrit measurements. In the hands of an experienced operator, ultrasound is useful for rapid assessment of SGH at the bedside (Fig. 4). Head CT or MRI can provide a definitive diagnosis, but may not be practical in the acute setting, and treatment should not be delayed while awaiting CT or MRI if suspicion for SGH is high. Findings of decreasing hematocrit, increasing FOC, and/or tachycardia, are consistent with ongoing blood loss, for which central access via umbilical vessel catheterization should be obtained for the administration of volume expanders and monitoring of blood pressure. Volume expansion is provided with normal saline, whole blood, or packed red blood cells (PRBCs) [see section 3.1]. In a retrospective review of the use of emergency uncrossmatched blood transfusions during neonatal stabilization, Finn, et al. noted SGH as the indication for four of the thirty-nine newborns who received emergency transfusions [20]. Coagulation studies should be obtained due to the risk of consumptive coagulopathy with large bleeds, with transfusion of fresh frozen plasma, cryoprecipitate, and platelets as indicated. Case reports have shown administration of recombinant activated factor VII to be an effective therapy for infants with massive subgaleal hemorrhage [37,38].

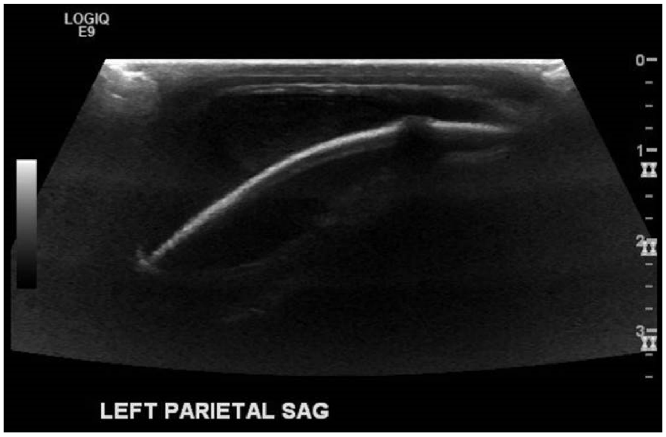

Fig. 4. Ultrasound view of subgaleal hemorrhage. Note fluid extending beyond the suture line. Courtesy of Amy Mehollin-Ray MD.

5. Nerve palsies

Peripheral nerve palsies are a frequently described sequelae of birth injury. The three most often reported peripheral nerve injuries due to birth trauma are: 1) facial nerve palsy (incidence 0.1–0.7% of births [39]), 2) brachial plexus palsy (incidence 0.03–0.2% of births [40]), and 3) phrenic nerve palsy. Of these, phrenic nerve injury poses the highest risk of morbidity and mortality due to concomitant paralysis of the diaphragm. The incidence of phrenic nerve injury is reported to be 1:15,000 to 1:30,000 live births, with an estimated 10–15% mortality rate [41,42]. Affected newborns may require urgent intervention shortly after delivery due to significant respiratory distress.

5.1. Mechanism of injury

The phrenic nerve originates from the anterior rami of the cervical 3 through 5 (C3–C5) nerve roots and descends through the thorax to innervate the diaphragm. The phrenic nerve is the only source of motor innervation to the diaphragm, hence it plays a crucial role in breathing. The motor innervation activation allows the diaphragm to contract with inspiration, resulting in a flattened diaphragm and decreased intrapleural pressure, with relaxation and return to the dual dome shape during exhalation. Phrenic nerve injury due to birth trauma typically occurs when there is stretching or avulsion of the C3–C5 nerve roots due to extreme lateral flexion and traction of the neck at birth [43].

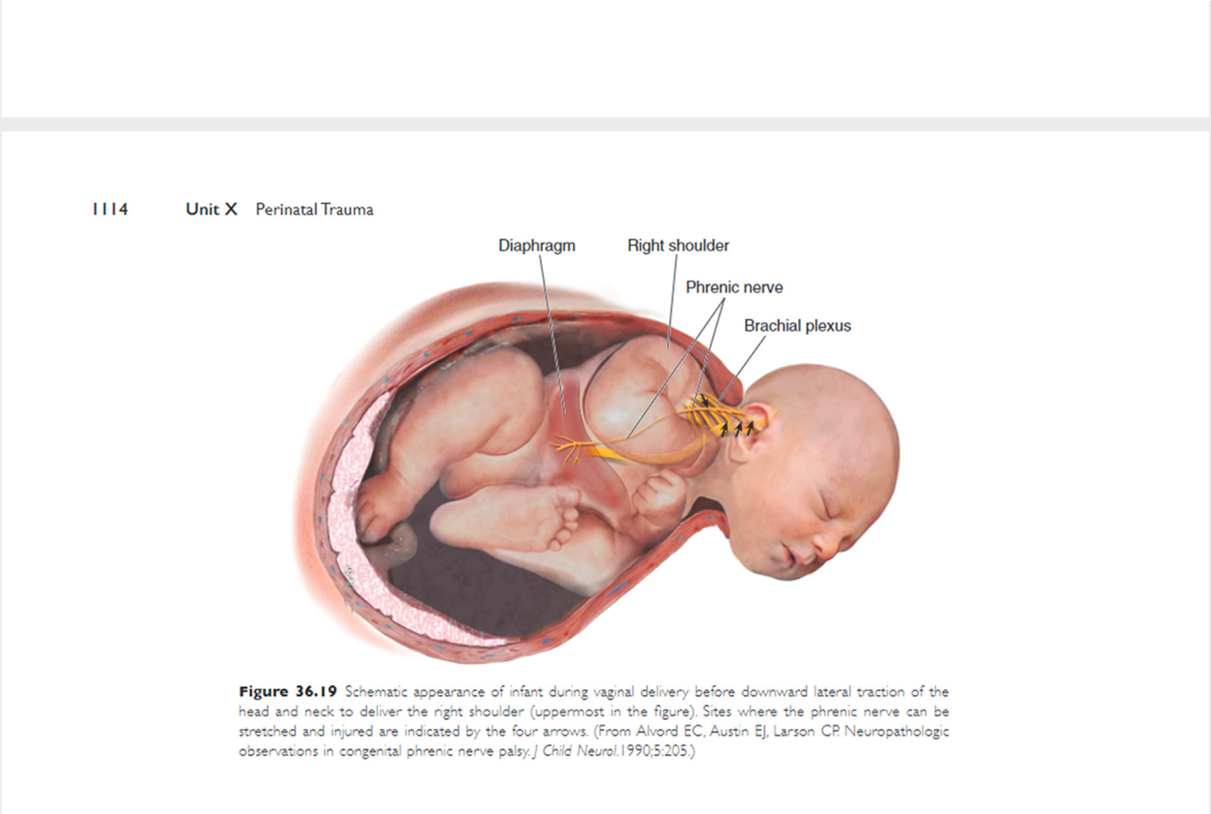

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Figure 36.19 Schematic appearance of infant during vaginal delivery before downward lateral traction of the head and neck to deliver the right shoulder (uppermost in the figure). Sites where the phrenic nerve can be stretched and injured are indicated by the four arrows. (From Alvord EC, Austin EJ, Larson CP. Neuropathologic observations in congenital phrenic nerve palsy. *J Child Neurol.* 1990;5:205.)

Fig. 5. Diagram illustrating mechanism of injury to brachial plexus and phrenic nerve due to downward lateral traction of head and neck during delivery From: Alvord EC, Austin EJ, Larson CP. Neuropathologic observations in congenital phrenic nerve palsy. J Child Neurol 1995; 5:205 Used with permissions from Elsevier [73].

Given the close proximity to the brachial plexus, a large majority of cases of neonatal diaphragmatic paralysis are associated with brachial plexus injury (Fig. 5). Approximately 80%–90% of newborns with diaphragmatic paralysis have an associated brachial plexus injury [42]. Conversely, a small percentage of newborns who present with a brachial plexus palsy will have concomitant phrenic nerve injury. A retrospective medical record review of 166 newborns with brachial plexus palsy reported a 2.4% incidence of concurrent phrenic nerve injury [44]. In another review of 191 babies with brachial plexus injury, Al-Qattan reported a 4.2% incidence of concurrent phrenic nerve palsy [45].

5.2. Risk factors

The risk factors for phrenic nerve injury are consistent with those described for all birth injuries and include fetal macrosomia, instrumented delivery, shoulder dystocia, and vaginal breech delivery (Fig. 6). Shoulder dystocia poses the greatest risk for brachial plexus injury, with Foad et al. reporting a 100 times greater risk of brachial plexus injury when delivery was complicated by shoulder dystocia [46]. The reported incidence of brachial plexus injury secondary to shoulder dystocia varies widely and ranges from 4% to 40% in the literature [47]. Vaginal breech delivery in particular has been associated with phrenic nerve palsy in several publications [48–50]. In a more recent analysis of 14 neonates with phrenic nerve injury, Stramrood, et al. noted that 57% of affected infants had a breech delivery [41].

Management/Treatment: Life-threatening respiratory compromise may result from phrenic nerve injury, requiring interventions to stabilize the infant in the delivery room setting. Phrenic nerve injury should be considered for newborns with acute respiratory distress at birth, particularly if the delivery was complicated by shoulder dystocia, brachial plexus injury is noted on exam, or if other risk factors exist for birth injury (macrosomia, use of instrumentation, etc). Low Apgar scores often accompany phrenic nerve injury [41], which is not unexpected given the association with difficult delivery and shoulder dystocia, and infants may require resuscitation at delivery. Phrenic nerve palsy can cause severe respiratory failure because of the newborn's relatively low reserve in respiratory function, relatively weak intercostal muscles, and high dependency on abdominal respiration [51]. Affected infants can exhibit paradoxical or see-saw breathing, tachypnea, and cyanosis soon after delivery, and symptoms will be more severe when paralysis is bilateral. Injury is bilateral in approximately 10% of cases, and unilateral in approximately 80% of cases, with the right side affected more often than the left [41,42]. Paralysis is ipsilateral thus, if accompanied by brachial plexus injury, careful examination of the newborn may reveal diminished breath sounds on the same side as the brachial plexus palsy. Chest radiograph (CXR) reveals elevation, or eventration, of the diaphragm on the affected side (Fig. 7), however, CXR may appear normal if the newborn is receiving positive pressure ventilation. Ultrasound, the preferred method of diagnosis because it does not utilize radiation, demonstrates lack of or paradoxical diaphragmatic movement and is helpful in confirming the diagnosis (Fig. 8). Initial treatment focuses on the acute management of respiratory symptoms, and may include supplemental oxygen and continuous positive airway pressure. Severely affected infants, typically those with bilateral paralysis, will require endotracheal intubation and mechanical ventilation, often in the delivery room setting. Plication of the diaphragm is recommended for infants who are unable to wean from respiratory support, or for infants with persistent respiratory distress leading to failure to thrive. Timing of plication varies in published case reports [41,48,51,52], although, in the majority of cases, plication is successful and infants are able to be weaned from respiratory support shortly thereafter.

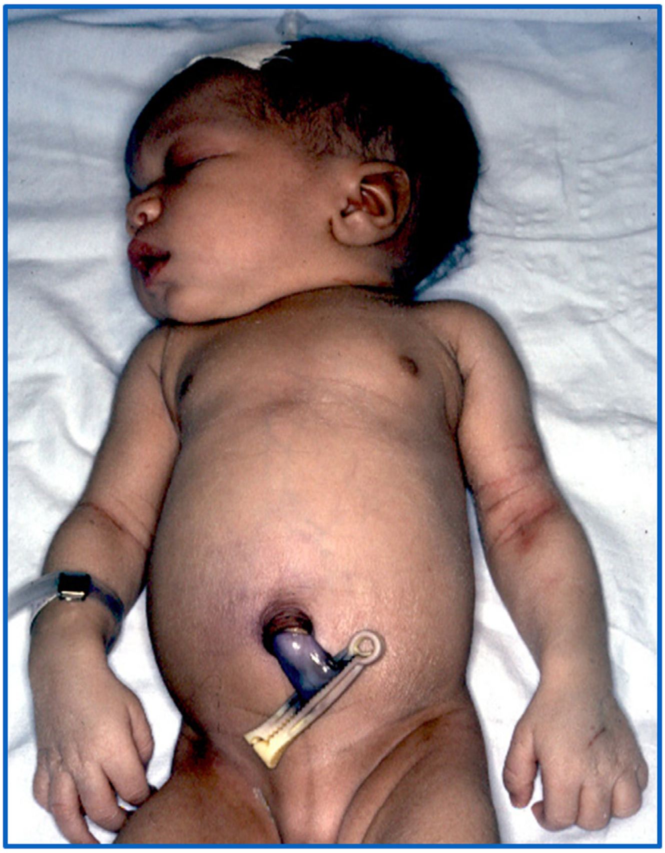

Fig. 6. Newborn with flaccid upper extremities due to bilateral brachial plexus injury. Photo courtesy of Gerardo Cabrera-Meza MD.

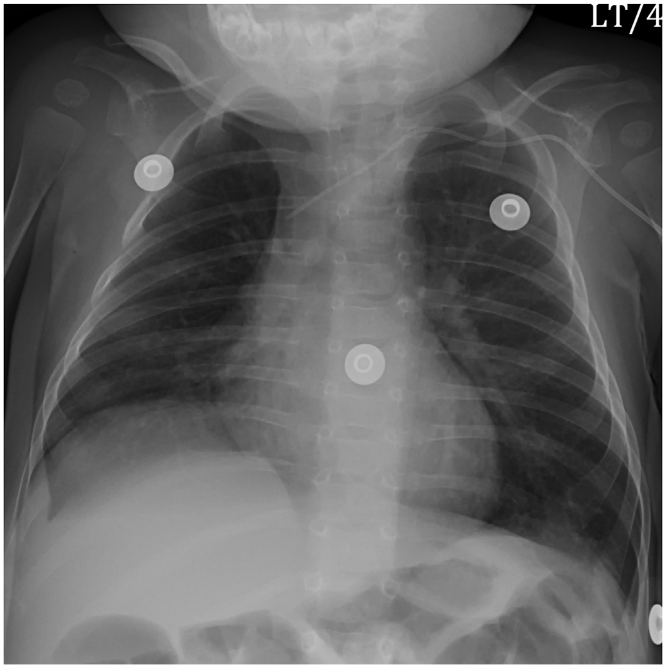

Fig. 7. Paralysis of right diaphragm Photo courtesy of: Amy Mehollin-Ray MD.

6. Spinal cord

Although quite rare and usually catastrophic, spinal cord injuries due to birth trauma require urgent management in the delivery room setting. Injury to the upper cervical spinal cord is more common than injury to the lower cervical and thoracic spinal cord. The true incidence of birth-related spinal cord injury is difficult to determine, with the majority of incidence-specific data being published in the 1990s. In a review of 15 cases occurring over a span of thirteen years, the incidence of high cervical spinal cord injury was estimated at 0.15 per 10,000 live births [53], while an earlier publication by Rehan and Seshia reported an incidence of 0.34 per 10,000 (1 in 29,000) live births complicated by serious spinal cord injury [54].

6.1. Mechanism of injury and risk factors

Spinal cord injury due to birth trauma is the result of excessive traction or rotational forces on the spine during difficult delivery. The neonate in particular is susceptible to spinal cord injury due to lax ligaments, weak muscles, and incomplete mineralization of the vertebrae, which can allow the spine to stretch further than the spinal cord [55]. Injuries described in the literature include hematomyelia (intramedullary spinal cord hemorrhage), extraspinal hematoma, disruption or transection of the spinal cord, and malalignment or dislocation of the spine [56,57]. Similar to other birth injuries, vaginal breech delivery and instrumented (forceps) delivery are the most commonly cited risk factors for birth-related spinal cord injuries. Upper cervical spine lesions are typically associated with vertex delivery, while lower cervical and thoracic spine injuries (cervicothoracic) are often associated with breech delivery. Forceps rotation during vertex delivery – specifically, rotation of 90° or more from occipitoposterior or occipitotransverse position – has been shown to be a major risk factor for high cervical spine injury (above C4), as demonstrated in a review of 15 cases of upper spinal cord injury by Metigolgou et al. in which the delivery of 14 of the 15 affected neonates involved forceps rotation [53]. Vaginal breech delivery assumes an increased likelihood of lower cervical and thoracic spine injury due to application of excessive pulling forces to achieve delivery of an entrapped head (Figs. 9 and 10). In a retrospective review of 22 neonates with spinal cord injury, all fourteen patients with upper cervical spinal cord injury had vertex presentations, and the six patients with cervicothoracic spinal cord injury all had a breech presentation [58].

Management/Treatment: Depending on the level of spinal cord insult, affected neonates may present at birth with hypotonia, flaccid tetraplegia or flaccid paraplegia, respiratory distress, or apnea. Other birth related injuries may also be evident, such as brachial plexus palsies, or fractures. When risk factors and initial presentation raise the possibility of spinal cord injury, the newborn's head, neck and spine must be immobilized as soon as possible after delivery. Personnel skilled in neonatal resuscitation and endotracheal intubation should be available at delivery, as neonates with lesions above C4 will likely have apnea in the delivery room [53] (Fig. 11). Ultrasound should be urgently obtained at bedside to assist with the diagnosis. In addition to easy access and fast results, ultrasound is the preferred imaging modality due to incomplete ossification of the posterior vertebral arch which allows for visualization of intra- and extra spinal lesions, as well as spinal disruption and malalignment [54,57]. Vertebral fractures or spinal dislocations may accompany the injury, hence frontal and lateral radiographs of the spine should be obtained to identify neonates with these injuries, as some may be amendable to surgical therapy [25,42,56]. Magnetic resonance imaging (MRI) should be obtained early if the nature of the lesion is not clear, and to differentiate between edema, ischemia, or hemorrhage [25]; however, a normal early MRI must be cautiously interpreted as it does not necessarily rule-out spinal cord injury [54,58]. MRI done after the acute phase of injury can be useful to predict long term prognosis. Newborns with upper cervical spinal cord injury have been shown to have worse outcomes than those with cervicothoracic and lower spinal cord injury [56,58]. MacKinnon et al. noted a 50% mortality rate in their analysis of 22 cases of birth-related spinal cord injury, with significant morbidity (ventilator dependency, paraplegia) in the majority of survivors. Age of first

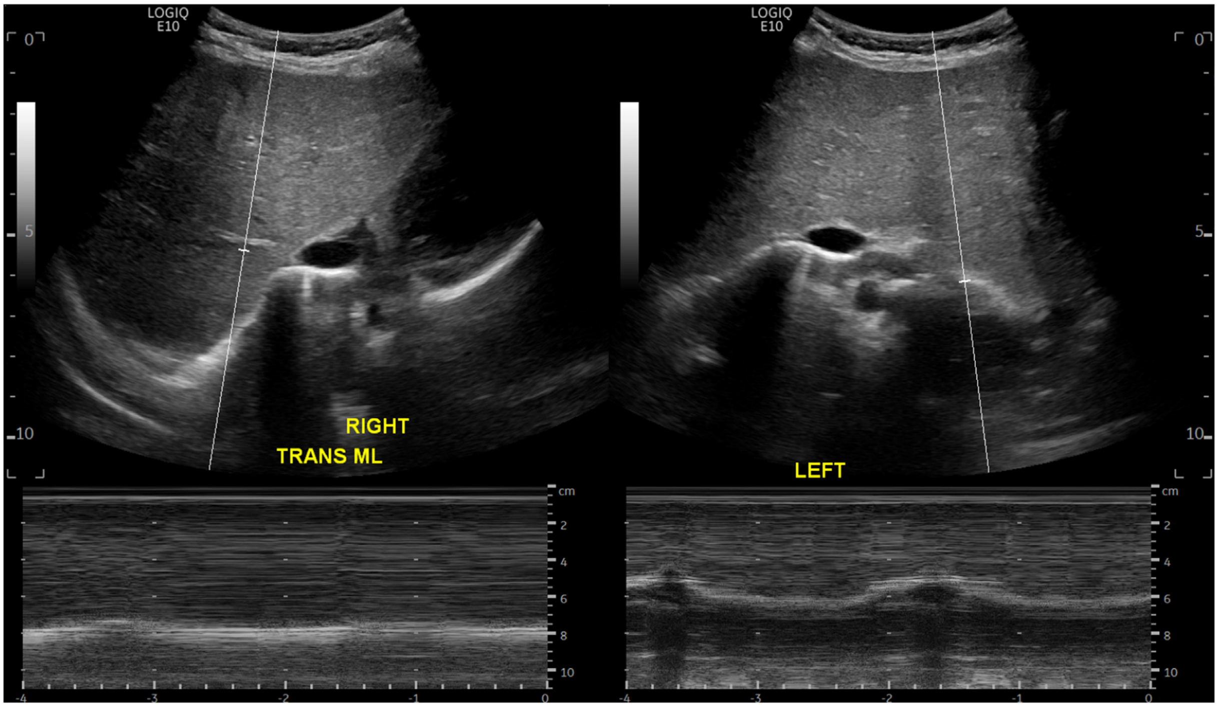

Fig. 8. US images for patient in Fig. 7. Term infant with hypotonia, poor feeding, respiratory concerns. R diaphragm persistently elevated on CXRs, M-mode US shows paralysis of R diaphragm, normal motion of L Courtesy: Amy Mehollin-Ray MD.

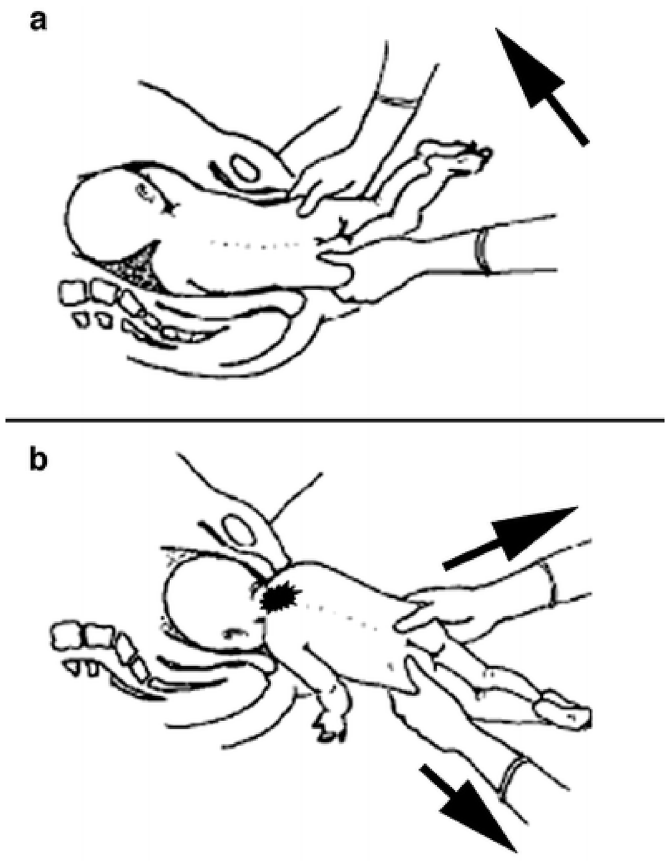

Fig. 9. Mechanism of spinal cord injury during vaginal breech extraction with fetal head entrapment with excessive traction maneuvers. From: Vialle R, Piétin-Vialle C, Vinchon M, Dauger S, Ilharreborde B, Glorion C. Birth-related spinal cord injuries: a multicentric review of nine cases. Childs Nerv Syst 2008; 24(1):79–85. Used with permissions.

spontaneous breath and rate of recovery of motor function in the first three months were noted to be outcome predictors [58].

7. Visceral injury

Injuries to intra-abdominal organs are a rare consequence of birth trauma and can be acutely life threatening due to the risk of organ rupture and severe hemorrhage. These injuries may initially go unnoticed due to lack of visible signs of trauma. Injuries to the liver, spleen, and adrenals have been reported in the literature, with hepatic injury occurring more often than injury to other organs. The incidence of hepatic injury due to birth trauma is unknown, with estimations in the literature based on series from several years ago where subcapsular liver hematoma or hemoperitoneum were noted at the time of autopsy [59,60]. Adrenal hemorrhage is less common than hepatic injury, but occurs more often than splenic injury. Published studies in which several thousand newborns were screened with abdominal ultrasound in the first few days after birth report an incidence of adrenal hemorrhage of 1.9–2.8 per 1000 deliveries [61,62]. Splenic injury is rare in the newborn and precise incidence is unknown, with less than fifty cases reported in the world's literature as of the year 2000 [63].

7.1. *Mechanism of injury and risk factors*

Several risk factors for birth-related injury to intra-abdominal organs have been identified. As with the previously described birth traumas, macrosomia, breech delivery, “difficult delivery”, and use of instrumentation have been associated with injury to abdominal organs [64]. Compression of the thorax during delivery can cause direct injury to the liver in the area where the costal margin of the rib cage comes in contact with the anterior hepatic surface; compression on the chest can also force the liver downward and cause tearing at the ligamentous peritoneal insertion [65]. Resuscitation at delivery with chest compressions has also been identified as a risk factor for liver injury due to the liver's superficial location adjacent to the heart [64]. The liver is not fully protected by the rib cage in neonates, with a normal anatomic location of up to three centimeters below the right costal margin. These

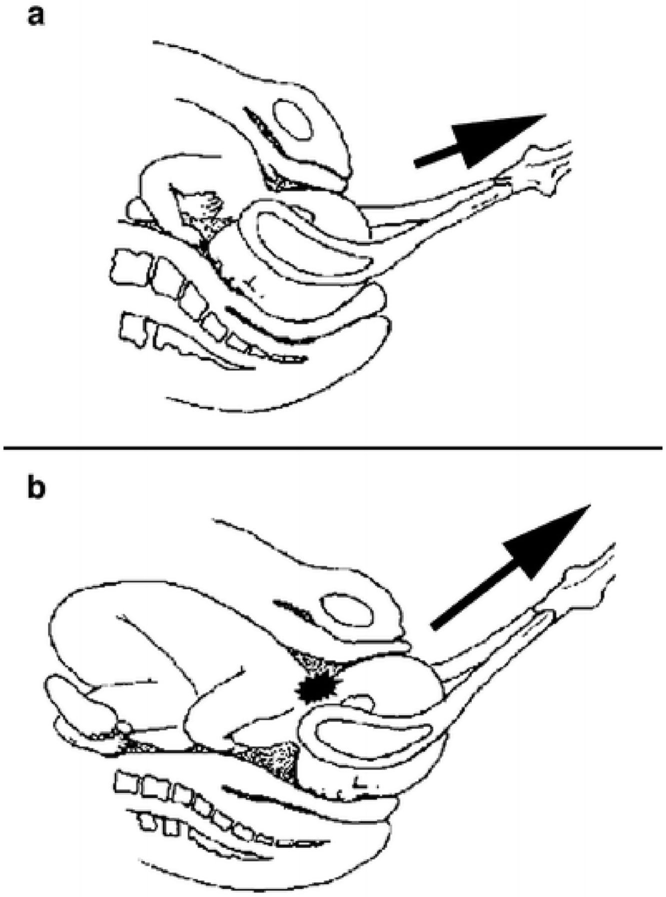

Fig. 10. Mechanism of spinal cord injury forceps assisted vaginal delivery demonstrating possible stretch injury due to excessive traction forces from the forceps. From: Vialle R, Piétin-Vialle C, Vinchon M, Dauger S, Ilharreborde B, Glorion C. Birth-related spinal cord injuries: a multicentric review of nine cases. Childs Nerv Syst 2008; 24(1):79–85. Used with permissions.

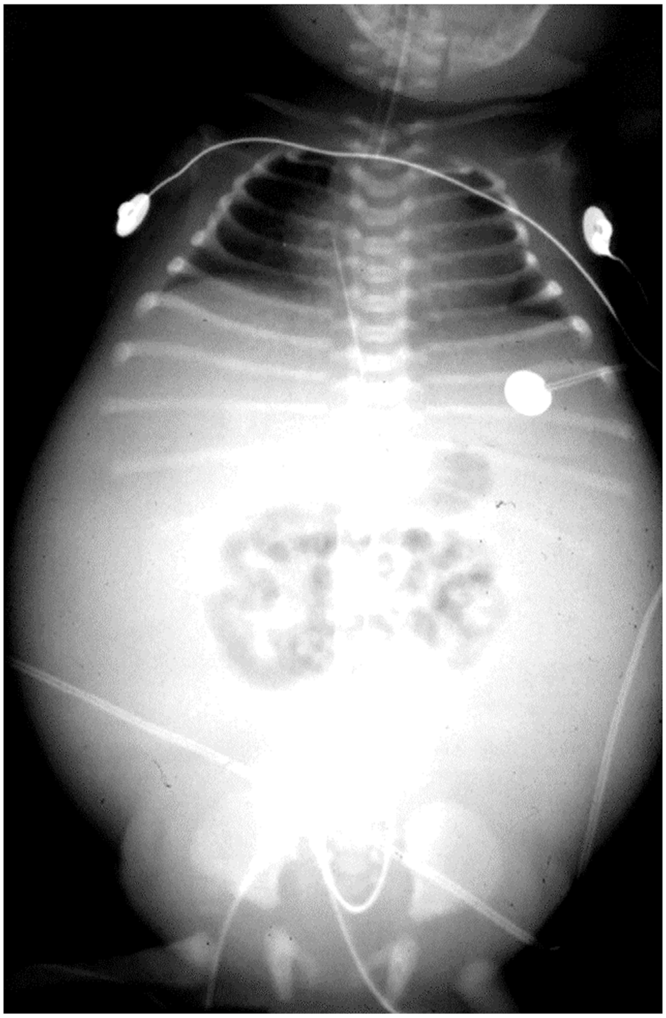

Fig. 11. X-ray demonstrating spinal cord transection at level above C4. Newborn is intubated. Photo courtesy of: Gerardo Cabrera-Meza MD.

factors, in addition to a friable consistency, contribute to the susceptibility of the liver to injury, particularly in premature infants [60]. Similar mechanisms have been proposed for birth-related injury to the spleen. However, unlike the liver, the anatomic locale of the spleen in the left upper quadrant of the abdomen, between the fundus of the stomach and the diaphragm, offers protection against injury during the birth process [66]. The adrenal glands are relatively large and highly vascularized in the neonatal period, features that contribute to the susceptibility of the gland to trauma during delivery [67]. Risk factors most often associated with neonatal adrenal hemorrhage are traumatic vaginal delivery and macrosomia, with the right side more often injured than the left, likely due to compression of the gland between the liver and the spine [68]. In a retrospective study of over 26,000 newborns screened with abdominal ultrasound on day two of age, macrosomia (birth weight > 4 kg) was noted in 21% of the newborns with adrenal hemorrhage [62]. Unilateral adrenal gland injury is more common than bilateral, with bilateral hemorrhage occurring in 5–15% of cases [69].

Management/Treatment: Solid organ injury may occur in two phases, 1) initial subcapsular hemorrhage follow by, 2) rupture of the hematoma with resultant hemoperitoneum. Neonates with solid organ hemorrhage that remains contained within the capsule may have a delayed presentation, with symptoms of anemia (tachycardia, tachypnea, poor feeding) emerging several days after the injury. Conversely, neonates with solid organ rupture present with acute decompensation, sudden pallor, and the classic triad of shock, anemia, and bluish discoloration of the abdomen [55]. Rupture of the liver occurs far more commonly than splenic rupture, although both have been well described in the literature and both constitute a life-threatening emergency for the neonate [64,66,70,71]. Depending on the severity of the injury and rate of bleeding, neonates may present in the delivery room or within hours of delivery, as the hematoma tends to increase up to 4–5 cm prior to rupture into the peritoneal cavity [64]. Abdominal ultrasound at the bedside is a rapid diagnostic tool and should allow differentiation of blood from other forms of ascites [66]. Computed tomography (CT) can be obtained to confirm the source of bleeding, if the neonate is stabilized sufficiently for transport to the CT scanner. In the event of subcapsular rupture, rapid diagnosis and immediate treatment are crucial to reducing morbidity and mortality. Treatment includes aggressive management of hypovolemic shock, and clotting factor replacement as indicated [70]. Volume resuscitation with blood is preferable, although an isotonic crystalloid solution such as normal saline can be used while awaiting the arrival of blood [see section 3.1]. Persistent coagulopathy is treated with fresh frozen plasma, cryoprecipitate, or platelet transfusion if warranted. Conservative management with correction of coagulopathies, blood transfusion, and serial/intensive monitoring is preferred to surgical intervention, although some infants will require laparotomy if bleeding continues despite these efforts [55,63,70]. Splenectomy, previously the standard of care for neonates with splenic rupture, is to be avoided when possible due the increased risk of postsplenectomy sepsis. Successful nonsurgical management of splenic rupture has been reported [63,72]. Nonsurgical management of adrenal hemorrhage is the standard, with spontaneous resolution reported in the majority of cases

[69]. Although adrenal insufficiency as a sequelae of hemorrhage is rare, it has been reported in infants who sustained bilateral injury. In an analysis of 74 neonates with adrenal hemorrhage, Gyurkovits, et al. noted adrenal insufficiency in one infant who had sustained bilateral hemorrhage [62]. Likewise, Zessis et al. report a case of bilateral hemorrhage with subsequent adrenal insufficiency requiring persistent therapy in a newborn with macrosomia and traumatic vaginal delivery [68].

8. Conclusion

Birth injuries with the potential for significant morbidity and mortality must be identified as soon as possible after delivery, and treatment should follow within minutes to hours after birth to ensure the best possible outcome for the neonate. A medical team trained in newborn resuscitation, including persons with advanced resuscitation skills including endotracheal intubation and umbilical vessel catheterization, should be available for every delivery for which there are risk factors for birth trauma.

Declaration of competing interest

The author has no conflicts of interest.

Practice points

- Risk factors for birth trauma are: instrumented delivery, vaginal breech extraction, fetal macrosomia, maternal obesity, and shoulder dystocia.
- Life-threatening birth injuries are rare, require treatment within minutes to hours after delivery, and include: cranial hemorrhage, diaphragm paralysis, spinal cord injury, and visceral injuries.
- Whole blood is the preferred treatment for acute hemorrhage in the neonate, and O-Rhesus-negative, uncrossmatched blood can be given in the acute setting.
- Bedside ultrasound can be useful for rapid evaluation of birth injuries, however MRI or CT may be needed to confirm the diagnosis.
- Intra-abdominal bleeding should be considered for neonates who present with shock, pallor, anemia, and abdominal distension.

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Surgical management of critical congenital malformations in the delivery room

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A B S T R A C T

Newborn emergencies that occur in the delivery room are frequently the result of life-threatening congenital anomalies that can result in death or severe disability if not treated in the immediate postnatal period. Prompt recognition and treatment of such disorders are paramount to ensuring the wellbeing of the infant. As congenital anomalies are frequently being diagnosed earlier due to improved prenatal detection, the coordination of planned interventions for life-threatening malformations is also becoming more common. This article serves as a guide for the presentation and initial management of the most common non-cardiac, newborn surgical emergencies.

1. Introduction

Various life-threatening congenital anomalies may present in the delivery room or shortly thereafter. These anomalies require prompt recognition by both obstetricians and pediatricians given that delayed intervention may result in permanent disability or even death. With recent advances in prenatal detection of congenital malformations over the past several decades, many of these disorders are routinely detected by fetal ultrasound, thereby alerting clinicians early to their presence. In such cases, consultation with an experienced team including perinatologist and pediatric surgeon should take place as early as possible to ensure the availability of specialized personnel and resources to appropriately intervene on these potentially life-threatening malformations in the delivery room. The following summary provides an overview of the most common non-cardiac congenital anomalies that require immediate intervention following birth.

2. Airway obstruction

2.1. Pierre Robin sequence

Pierre Robin sequence may occur in isolation or as part of several other congenital anomaly complexes and syndromes. Although this condition has multiple etiologies, its hallmark is the presence of a recessed, hypoplastic mandible. This leads to posterior displacement of the tongue causing upper airway obstruction. Additionally, the displacement can prevent fusion of the palatal shelves during early gestation, which results in a cleft palate in the majority of cases [1]. Airway compromise can lead to hypoxia, cardiopulmonary arrest, pulmonary hypertension, and failure to thrive. Affected patients should be monitored to detect apnea and airway obstruction. Prone positioning is helpful to minimize airway obstruction, and insertion of a nasopharyngeal trumpet can protect the airway. In some rare cases, airway obstruction may be refractory to these measures and require endotracheal intubation or tracheostomy. Initially, feeding difficulties are also common and may necessitate placement of a nasogastric feeding tube and eventual surgical gastrostomy tube [1,2]. A trial of non-operative measures should be utilized in these patients as with time most infants are able to keep their tongue away from the larynx and mandibular growth during the first year of life allows for resolution of airway problems in a majority of patients. Other surgical options include distraction of the mandible, in which fracture of the mandible is performed and an external fixator is used to open the oral passage. This approach has the benefit of permanently changing mandibular size to create adequate space for the tongue, allowing many patients to avoid tracheostomy altogether when performed early [3].

2.2. Congenital high airway obstruction syndrome (CHAOS)

Congenital high airway obstruction syndrome (CHAOS) is characterized by complete or near-complete upper airway obstruction due to atresia, membranous webs, or stenosis of the larynx or trachea (Fig. 1). Cases of atresia present with asphyxia at the time of birth and require emergent tracheostomy. The diagnosis can be made prenatally via ultrasonographic findings of large echogenic lungs, dilated distal trachea, and flattened hemidiaphragms. If diagnosed prenatally, an Ex

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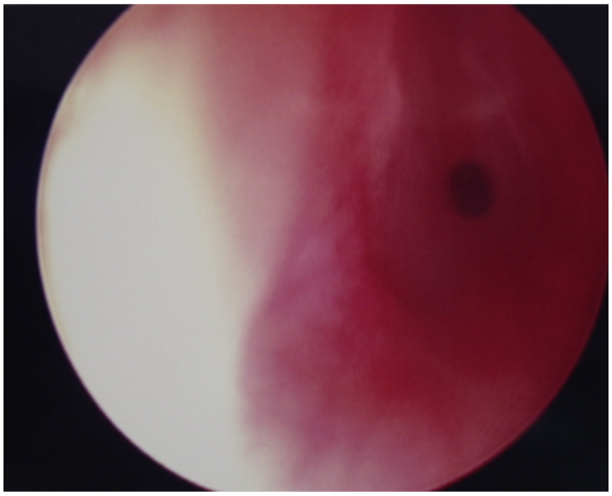

Fig. 1. Bronchoscopic view of trachea in infant with CHAOS diagnosed at birth and treated with emergent bedside tracheostomy. Patient also had associated type C esophageal atresia repaired during first week of life and eventually underwent tracheal reconstruction at a year of age.

Utero Intrapartum Treatment (EXIT) procedure with tracheostomy must be planned. Patients with webs or stenosis usually present during infancy with respiratory distress, stridor, and a weak or high-pitched cry. Depending on the degree of airway obstruction, some incomplete webs may be treated with simple lysis using endoscopic laser or sharp dissection, whereas more severe webs often require laryngeal reconstruction and tracheostomy [4]. Similarly, minor subglottic stenosis may be treated with an anterior cricoid-split or endoscopic division of cartilage with balloon dilation [5]. Congenital stenosis typically improves as the larynx grows, and fewer than half of children require tracheostomy.

2.3. Lymphatic malformations (cystic hygroma and lymphangioma)

Lymphatic malformations are benign lesions composed of dilated lymphatic channels or cysts. They are classified as macrocystic (previously cystic hygroma), microcystic (formerly lymphangioma), mixed or lymphovascular [6]. Macrocystic lymphatic malformations are composed of collections of large, interconnected lymphatic cysts lined by a thin endothelium. They present at birth as large, poorly delineated, translucent, soft masses covered by normal skin and are most commonly located in the cervicofacial region, axilla, or lateral chest wall (Fig. 2). They can be detected on prenatal ultrasound due to increased nuchal translucency and approximately half of cases are associated with chromosomal abnormalities such as Down syndrome. In contrast, microcystic lymphatic malformations may be present at birth or appear in the first few years of life. They are most frequently located in the proximal extremities, trunk, axilla, and oral cavity and present as a cluster of clear, translucent or hemorrhagic vesicles that can intermittently leak lymphatic fluid.

Although sclerotherapy is often successful in reducing the size of macrocytic lesions [7], surgical intervention may be needed at the time of birth if there is concern for airway compromise. Large neck lesions that are diagnosed prenatally may require an EXIT procedure in order to immediately secure the airway. If endotracheal intubation or tracheostomy is not possible, cannulation for extracorporeal membrane oxygenation (ECMO) may be required (Fig. 3). For lesions near the airway, an experienced pediatric surgeon should be consulted prenatally and be immediately available at the time of delivery.

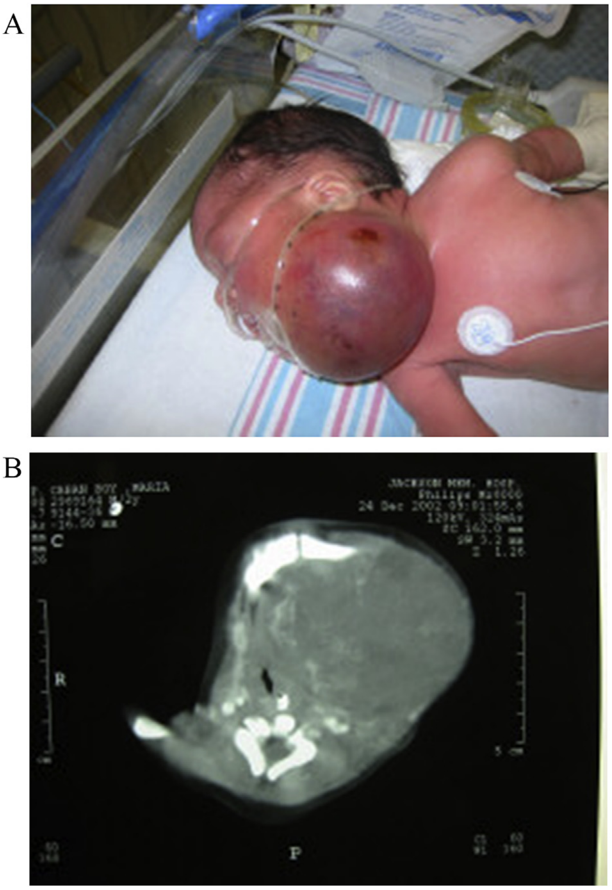

Fig. 2. Large lymphatic malformation in newborn infant (A). Computed tomography scan demonstrating compression of trachea (B).

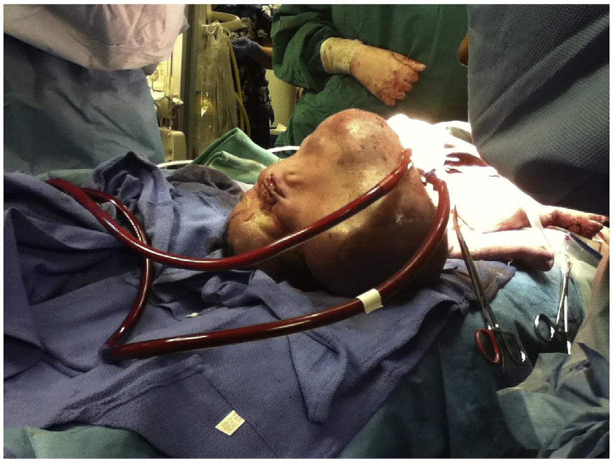

Fig. 3. Newborn infant with giant lympho-venous malformation treated with EXIT procedure for ECMO cannulation prior to surgical resection.

2.4. Mediastinal masses

Compression of the intrathoracic trachea or bronchi can also occur due to the presence of a mediastinal mass. A high-grade partial obstruction will result in air-trapping during exhalation with an over distended pulmonary lobe, whereas complete obstruction produces atelectasis. Compressive symptoms typically consist of tachypnea, wheezing, stridor, and cough. Teratomas of the anterior mediastinum are the most common cause in newborns [8]. These typically benign lesions can cause life-threatening respiratory distress requiring urgent surgical excision. The presence of calcifications on imaging studies is diagnostic for mediastinal teratoma. Additionally, lymphatic malformations can occasionally be located in the mediastinum (5%) and cause mass effect with compressive symptoms.

2.5. Double aortic arch

In double aortic arch, the paired aortic arch arteries fail to remodel appropriately, which results in two aortic arches completely encircling the trachea and esophagus prior to rejoining posteriorly to form the descending aorta. The most common presenting symptoms are due to tracheal compression and include stridor, wheezing, cough, and respiratory distress [9]. Esophageal symptoms are also common and include difficulty feeding and vomiting. Clinicians must have a high index of suspicion given the rarity of double aortic arch, and the diagnosis can usually be confirmed by echocardiography. Treatment involves thoracotomy, or video-assisted thoracoscopy (VATS) where available, with ligation and division of the smaller aortic arch and patent ductus arteriosus.

3. Bronchopulmonary malformations

3.1. Bronchogenic cysts

Bronchogenic cysts arise from anomalous budding during development and can occur throughout the tracheobronchial tree but are most commonly located near the carina [10]. Although rare, these lesions are among the most common lower respiratory tract malformations. Affected patients typically present as older children with recurrent pneumonia, but they may become symptomatic during infancy. Newborns with rapidly enlarging central cysts can develop compressive symptoms consisting of respiratory distress, cyanosis, and feeding difficulty that necessitate early surgical excision (Fig. 4).

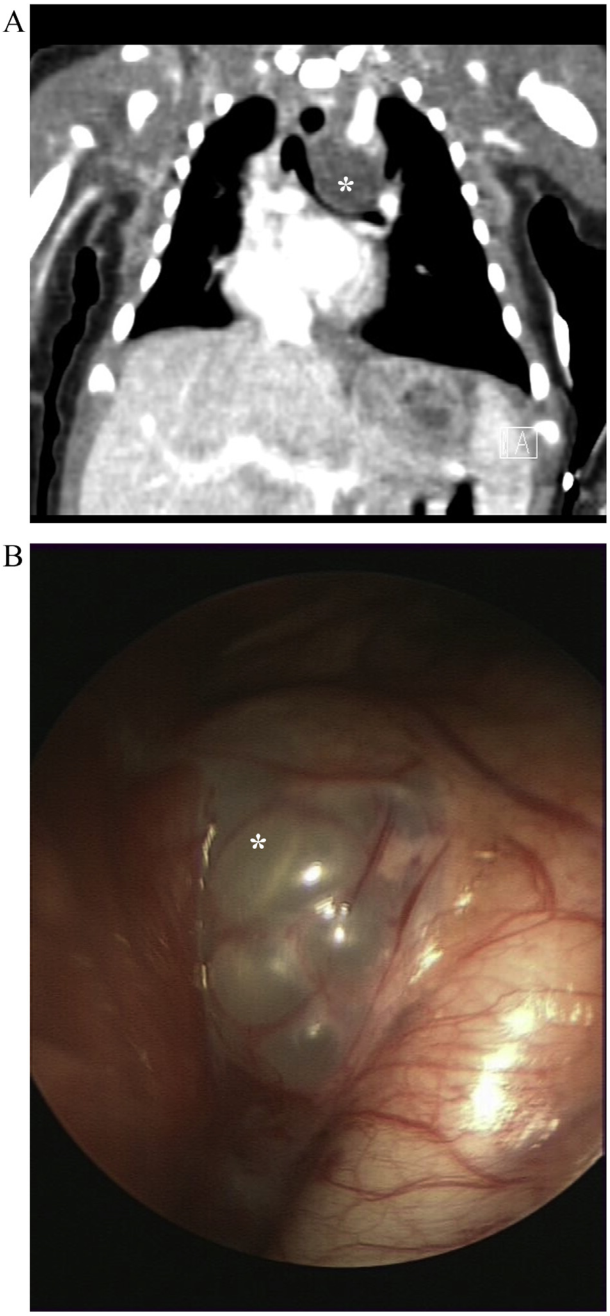

Fig. 4. Computed tomography scan of patient with bronchogenic cyst causing compression (*) of left mainstem bronchus (A). Thoracoscopic view of bronchogenic cyst (*) medial to aortic arch during resection (B).

3.2. Congenital pulmonary airway malformation

Congenital pulmonary airway malformation (CPAM), previously known as congenital cystic adenomatoid malformation (CCAM), is the most common developmental anomaly of the lung [11]. Affected patients may present with respiratory distress in the newborn period. These lesions are often detected during routine prenatal ultrasound. Twenty-five percent of newborns with a prenatal diagnosis of CPAM are symptomatic at birth, and the likelihood of respiratory distress increases with the size of the lesion [12]. Fetuses with large CPAMs and/or hydrops have an especially poor prognosis. In these cases, treatment options include antenatal corticosteroids, drainage procedures, fetal surgery, or early delivery. In the postnatal period, the diagnosis of CPAM in a newborn with respiratory distress may be suggested by a chest radiograph demonstrating a hyperlucent lobe with midline shift. However, plain radiographs can often fail to detect these lesions. Therefore, all symptomatic newborns with a prenatal diagnosis of CPAM should also undergo advanced thoracic imaging with contract-enhanced computed tomography (CT) or magnetic resonance imaging (MRI). For asymptomatic patients, delayed imaging can be obtained prior to elective resection of the lesion. Surgical resection is curative and has few complications. Lobectomy is generally preferred to wedge resection to ensure complete excision since the extent of some lesions may be difficult to identify intraoperatively.

3.3. Congenital lobar emphysema

Congenital lobar emphysema (CLE) results from progressive lobar hyperinflation due to a variety of disruptions in bronchopulmonary development. Although a definitive cause cannot be identified in approximately half of cases, the most frequently identified cause is obstruction of the developing airway, which occurs in 25% of cases [13]. This airway obstruction can be intrinsic or extrinsic, leading to the creation of a ball-valve mechanism of air trapping and hyperinflation. CLE is characterized by overdistention of one or more lobes of the lung. This leads to compression of the remaining lung tissue and potentially mediastinal shift. Affected infants are usually symptomatic in the neonatal period, with approximately 25–33% of cases presenting at birth, 50% by one month of age, and nearly all by six months of age [14]. Progressive respiratory distress develops rapidly in some infants, while others have a more gradual onset. The severity depends on the size of the affected lobe, the degree of compression of the surrounding lung tissue, and the extent of mediastinal shift [15]. The diagnosis can often be made from the characteristic appearance on chest radiograph, which typically demonstrates distension of the affected lobe, flattening of the ipsilateral hemidiaphragm, mediastinal shift, and compression of the

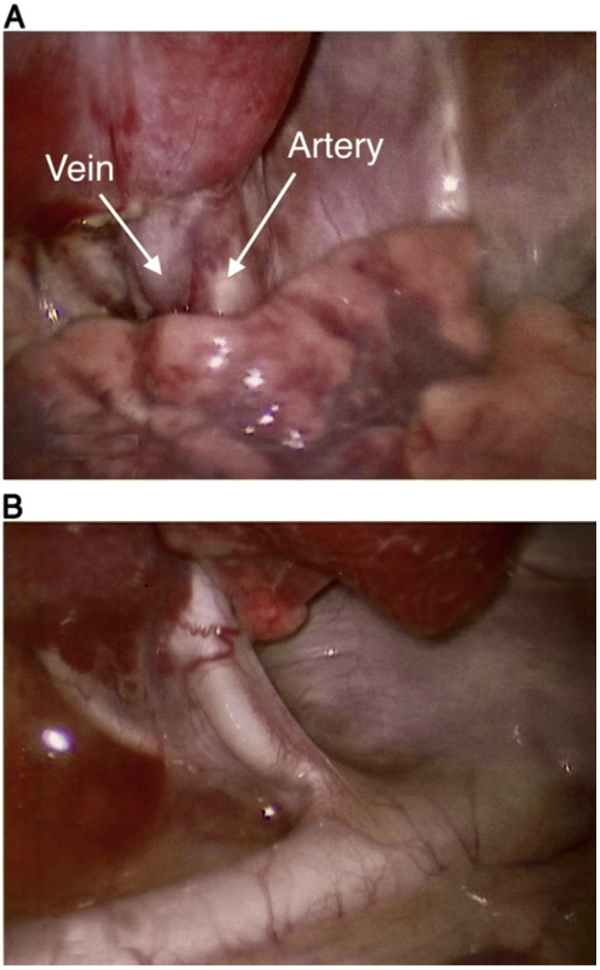

Fig. 5. Thoracoscopic view of left extralobar (A) and right intralobar (B) pulmonary sequestrations (superior to vessels). Used with permissions.

contralateral lung. CT or MRI may help establish the diagnosis and may demonstrate a source of airway obstruction. If the chest radiograph is obtained immediately after birth, the affected lobe may appear opacified due to retained fetal lung fluid. As the fluid is absorbed and the lobe becomes filled with air, progressive hyperinflation develops. CLE is sometimes detected by prenatal ultrasound but is often misdiagnosed as CPAM or bronchopulmonary sequestration [16]. Predictors of severe respiratory distress include polyhydramnios, fetal hydrops, and a decreased lung to thorax transverse area ratio (L/T value) [17]. The appropriate treatment of CLE in newborns with respiratory distress is surgical resection of the affected lobe.

3.4. Bronchopulmonary sequestration

Bronchopulmonary sequestration (BPS), also referred to simply as pulmonary sequestration, is a congenital abnormality of the lower airway that consists of a nonfunctioning mass of lung tissue. Although these lesions contain airway and alveolar elements, they lack normal communication with the tracheobronchial tree and receive their arterial blood supply from the systemic circulation (Fig. 5), which is of importance for distinguishing them from other lesions and planning their surgical excision [18]. The subtypes of BPS include intralobar sequestration, extralobar sequestration, hybrid BPS/CPAM lesions, and bronchopulmonary-foregut malformation. The most common subtype, intralobar sequestration, is located within a normal lobe and lacks its own visceral pleura. It typically has no bronchial connection to the proximal airway, but interalveolar connections (pores of Kohn) with the adjacent normal lung tissue can allow for the translocation of bacteria into the sequestration and cause recurrent infections, which is common for intralobar sequestrations. On the other hand, extralobar sequestrations are located outside of the normal lung and have their own visceral pleura, thereby lacking any intrapulmonary connections and rarely associated with infectious complications. Extralobar lesions can occasionally be extrathoracic located below the diaphragm in the retroperitoneum. Given that CPAM is the most common congenital anomaly of the lower airway, hybrid BPS/CPAM lesions comprise a substantial proportion of BPS [19]. These lesions have a blood supply from a systemic artery consistent with BPS, but they also have histologic features of CPAM. Bronchopulmonary-foregut malformation is a term used to refer to rare variants of BPS in which the sequestered lung tissue is connected to the gastrointestinal tract [20]. Many cases of BPS are initially detected by routine prenatal ultrasound, but may be difficult or impossible to distinguish from CPAM unless a systemic arterial blood supply can be identified. Ultimately, the final definitive diagnosis is only made by pathologic examination after surgical resection.

Most affected newborns are asymptomatic, but when symptomatic, BPS usually presents with respiratory distress at birth or shortly thereafter. Symptoms are more likely if the lesion is large, limiting the proper expansion of the adjacent normal lung. Later presentations are typically due to recurrent infections. For symptomatic newborns, those with a large lesion (occupying ≥20% of hemithorax) identified on ultrasound or plain radiographs, or those with risk factors for pleuropulmonary blastoma, early advanced cross-sectional imaging with CT or MRI is needed to confirm the diagnosis and define the aberrant vascular supply for preoperative planning. Early surgical resection of the affected lobe is indicated for these infants. For asymptomatic newborns without high-risk features, advanced thoracic imaging can be delayed up to six month of age to confirm the diagnosis and evaluate the need for elective surgical intervention [21]. Based on our institutional experience, we have developed and published a bronchopulmonary malformation surgical algorithm (Fig. 6) for the management of these malformations [22].

4. Esophageal atresia and tracheoesophageal fistula

Esophageal atresia (EA) and tracheoesophageal fistula (TEF) comprise a spectrum of relatively common congenital anomalies that typically occur together and are classified by their anatomic configuration. By far the most common form is type C, occurring in over 80% of cases. It consists of a blind proximal esophageal pouch and a distal TEF connecting the distal esophagus to the trachea [23]. The second most common variant is a pure EA, or type A, without any associated TEF. The other variants, in decreasing order of frequency, include TEF without EA (type E or "H-type"), EA with both a proximal TEF and a distal TEF (type D), and EA with only a proximal TEF (type B). The clinical presentation of TEF depends upon the presence or absence of EA. Given that EA is present in the vast majority of cases, polyhydramnios occurs in most pregnancies [24]. Nevertheless, many cases are not detected prenatally.

The majority of newborns with EA become symptomatic immediately after birth due to pooling of oral secretions resulting in excessive drooling, choking, respiratory distress, and inability to feed. A fistula between the trachea and distal esophagus leads to gastric distention and can result in aspiration pneumonia due to reflux of gastric contents through the TEF. The diagnosis of EA can be made by the inability to pass a nasogastric tube into the stomach and coiling of the catheter in the upper esophageal pouch, demonstrated on plain radiograph. A distal TEF may be suspected if radiographs also reveal a gas-filled gastrointestinal tract, whereas complete absence of intra-abdominal gas suggests the presence of EA without distal TEF. When the diagnosis is uncertain or a proximal TEF is suspected, a small amount of water-soluble, non-ionic, iso-osmolar contrast medium placed into the proximal esophageal pouch under fluoroscopic guidance will confirm

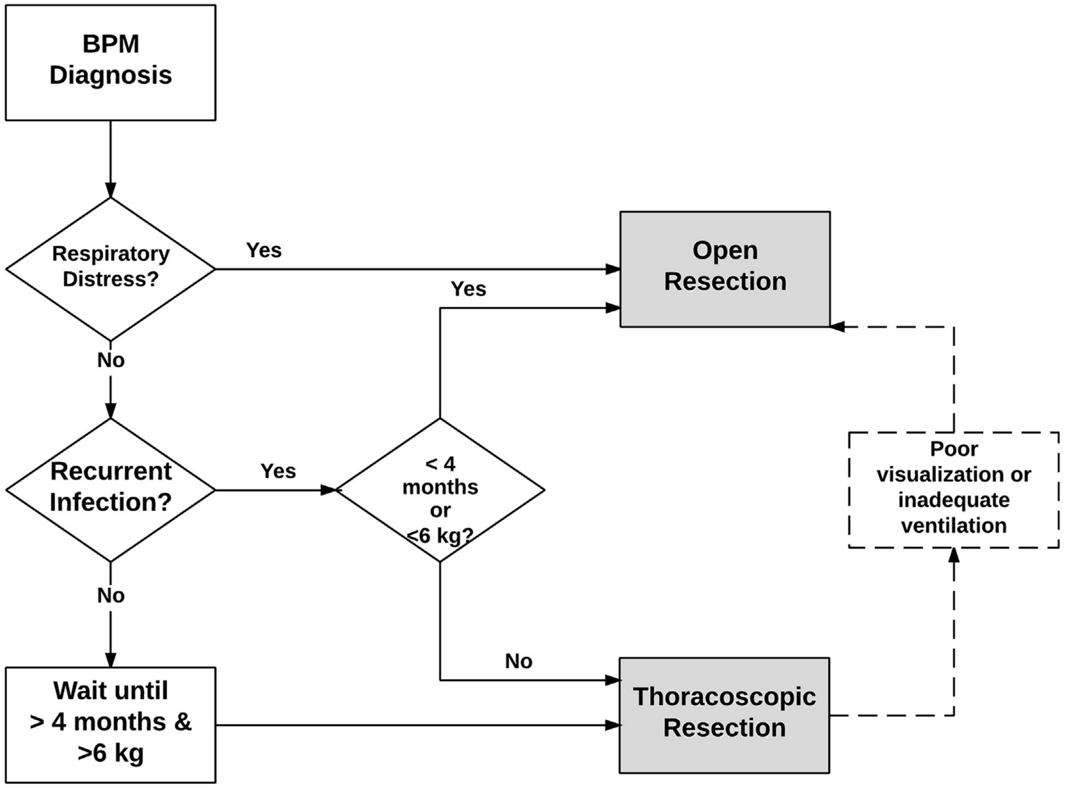

Fig. 6. Bronchopulmonary malformation surgical management algorithm utilized at Holtz Children's Hospital. Used with permissions.

the presence of EA. Barium contrast should be avoided as it can cause pneumonitis and granulomas if aspirated into the lungs. Patients with H-type TEFs may present early if the defect is large, with coughing and choking associated with feeding, but smaller defects of this type may not be symptomatic during the newborn period [25]. The diagnosis of H-type TEF (without EA) may not be evident on fluoroscopy and may require esophagoscopy and/or bronchoscopy to identify the fistula. Approximately one-half of cases of TEF and EA are associated with other anomalies, often as part of the VACTERL association (vertebral defects, anorectal malformation, cardiac defects, TEF, renal anomalies, and limb abnormalities), thus requiring further evaluation for additional anomalies [26].

The initial management for EA and TEF includes elevating the head to prevent aspiration of secretions, and decompression of the proximal esophageal pouch with a Replogle sump catheter. Routine endotracheal intubation should be avoided to prevent increased gastric distention from positive pressure ventilation, which can worsen pulmonary ventilation and even lead to gastrointestinal perforation. Preoperative echocardiography is necessary to rule out an anomalous right-sided aortic arch, as this finding may require a modified surgical approach. Early surgical intervention within the first few days of life is preferred for stable newborns of adequate birth weight.

The surgical treatment of TEF consists of ligation and division of the fistula. In cases of EA, primary anastomosis of the esophageal segments is preferred. A minimally invasive thoracoscopic approach is increasingly being utilized to minimize the morbidity associated with the traditional open thoracotomy [27]. Rarely, the distance between esophageal segments is too large for a primary anastomosis to be feasible, and surgical repair must be delayed for several months to allow for adequate esophageal growth to permit a primary repair. If this is unsuccessful, alternatives include elongation of the esophagus, interposition of jejunum or colon, or gastric transposition [28]. In preterm or very low birth weight infants (< 1500 g), surgical intervention within the first few days of life may be associated with increased morbidity, leading some pediatric surgeons to advocate for a staged approach with early ligation and division of the TEF followed by subsequent esophageal reconstruction at a later time [29,30]. In the setting of a delayed repair, early enteral access must be established for nutritional support. Feeding gastrostomy is rarely needed if early primary anastomosis is successful.

5. Congenital diaphragmatic hernia

Congenital diaphragmatic hernia (CDH) is a developmental defect of the diaphragm that allows abdominal viscera to herniate into the thoracic cavity. Due to direct compression of the ipsilateral lung and mediastinal shift and compression of the contra-lateral lung during development, there can be varying degrees of pulmonary hypoplasia and consequently, pulmonary arterial hypertension in the newborn. The vast majority of diaphragmatic defects are located posterior and lateral (Bochdalek hernia), with the remainder being anterior (Morgagni hernia), and rarely central. More than 80% of cases occur on the left side, and very rarely can be bilateral [31]. CDH is identified, or at least suspected, on routine prenatal ultrasound in more than half of cases. Affected neonates usually present in the first few hours of life with respiratory distress, although mild cases may not be identified until later in life. Physical findings include decreased or absent breath sounds on the affected side, a barrel-shaped chest, and a scaphoid-appearing abdomen due to migration of the abdominal contents into the thoracic cavity. On plain radiographs, the diagnosis of CDH can be quickly differentiated from large cystic anomalies of the lung by visualizing the course of a nasogastric tube that passes below the diaphragm with the tip curving back upward into the hemithorax within the herniated stomach.

When the diagnosis of CDH is made prenatally, or as soon as CDH is suspected after birth, patients who present with respiratory distress should be intubated immediately in the delivery room [32]. Bag-mask ventilation should be avoided to reduce gastrointestinal distention and further compression of the lung. The infant should be ventilated gently with low peak inspiratory pressures, employing permissive hypercapnia to minimize lung injury [32,33]. Delay in securing an adequate airway may contribute to acidosis and hypoxia, which increase the risk of pulmonary hypertension. A nasogastric sump tube should be placed in the stomach and connected to continuous suction to decompress the abdominal contents and reduce lung compression. The administration of surfactant therapy does not appear to improve outcomes in infants with CDH [34]. Similarly, inhaled nitric oxide does not appear to have long-term benefits, despite its widespread use for treating pulmonary hypertension in patients with CDH [33,34]. Other vasodilatory agents (e.g. sildenafil, treprostinil) have been shown to confer some improvement in severe pulmonary hypertension in a few case series [33]. Echocardiography should be performed early to determine the severity of pulmonary hypertension and detect any associated cardiac anomalies, as significant heart defects are frequently associated with CDH and confer a worse prognosis.

ECMO is considered for infants who remain severely hypoxemic despite maximal conventional ventilatory support, as these patients will not survive without it. Indications for ECMO include persistent hypoxia despite maximal ventilator support, hypotension refractory to fluid resuscitation and inotropic support, and inadequate oxygen delivery with persistent metabolic acidosis. There is no difference in survival between veno-venous (VV) and veno-arterial (VA) ECMO, although VV ECMO is associated with fewer neurologic complications [33,35]. Infants on ECMO are at risk for intracranial bleeding due to the need for continuous anticoagulation. Therefore, frequent transcranial ultrasound examinations are recommended for the duration of therapy given that ECMO is contraindicated in the setting of severe intracranial hemorrhage. Although ECMO allows for preoperative stabilization, its continuation may be required for weeks until the pulmonary hypertension improves. In a small group of patients with severe pulmonary hypoplasia and/or pulmonary hypertension, there may be no response to therapy of any kind, including ECMO, and support is often withdrawn.

The timing of surgical repair of CDH is dependent upon first stabilizing the neonate. In patients with only mild symptoms on minimal support without evidence of pulmonary hypertension or hypoplasia, repair can typically be performed safely at 48–72 h after birth. In those with mild pulmonary hypoplasia or reversible pulmonary hypertension, surgery is delayed until pulmonary function improves and pulmonary hypertension is resolved, allowing CDH repair after 5–10 days. Controversy exists over the timing of operative repair in patients who require ECMO, with some advocating repair of the defect while the infant is on ECMO and others recommending repair only once the infant has been weaned off of ECMO. Regardless of timing, the surgical approach consists of reducing the abdominal viscera and closure of the diaphragmatic defect. Ideally, the defect can be closed with a primary suture repair, but a prosthetic patch repair is often required in patients with large defects in whom increased tension using a primary repair compromises thoracic compliance [36]. If the abdominal wall is difficult to close following reduction of the hernia, the use of a temporary abdominal wall silo or patch may be needed with delayed abdominal wall closure [37].

6. Poland syndrome

Poland syndrome is a rare constellation of congenital limb anomalies consisting of chest wall and upper extremity abnormalities that typically affect only one side. It is characterized by the partial or complete absence of the costal cartilages of multiple ribs, chest wall muscles, breast tissue and nipple, as well as a high-riding scapula and digital abnormalities (e.g. brachydactyly, syndactyly) [38]. Although most patients do not have respiratory symptoms, those with severe chest wall deformities may experience respiratory failure requiring mechanical ventilator support. These infants may exhibit paradoxical respiratory movement of the chest wall, similar to that seen in flail chest, due to multiple missing or incomplete ribs (Fig. 7A and B). In such cases, early surgical intervention is necessary to stabilize the chest wall using polytetrafluoroethylene or titanium mesh (Fig. 7C) to bridge the gap between the hypoplastic ribs and sternum. As these children grow, they will require additional reconstructive surgery and further thoracoplasty.

7. Abdominal wall defects

7.1. Gastroschisis

Gastroschisis is a full-thickness abdominal wall defect associated with evisceration of the bowel and is typically located to the right of the umbilical cord insertion. Most cases can be detected by prenatal ultrasound by the end of the first trimester, and nearly all cases are associated with an elevated maternal serum alpha-fetoprotein level [39]. Given that cesarean delivery has not been shown to improve neonatal outcomes for uncomplicated gastroschisis [40], the mode of delivery should be selected based on the usual obstetric indications.

The initial management after birth consists of wrapping the exposed bowel in sterile saline dressings and covering it with a plastic organ bag to minimize ongoing fluid and heat loss. Intravenous fluids and broad-spectrum antibiotics should be administered, and an orogastric tube inserted to decompress the stomach. Most affected infants are born prematurely; therefore, special attention must be given to the neonate's respiratory status and thermoregulation.

Surgical management consists of reducing the bowel into the abdomen and primary closure of the abdominal wall defect as soon as possible. Although this approach is feasible within a few hours of birth for many patients [41], some require delayed closure when the bowel is unable to be fully reduced. The bowel often develops inflammatory changes due to the prolonged exposure to amniotic fluid, resulting in thickened, distended intestinal loops. A silastic silo is applied for these cases, and the eviscerated bowel is gradually reduced over several days until operative fascial or sutureless flap closure can be achieved. Patients are maintained on total parenteral nutrition (TPN) until they gain bowel function, as prolonged postoperative dysmotility is common.

The majority of cases occur in isolation without other associated congenital anomalies or aneuploidy, thus conferring favorable prognosis with survival rates greater than 90% [40]. However, gastroschisis can be complicated by the presence of intestinal atresia, stenosis, perforation, necrosis, or volvulus. The occurrence of these complications may be related to vascular disruption caused by herniated bowel and is associated with increased morbidity and mortality [42]. Nonetheless, the prognosis for infants born with gastroschisis generally remains favorable even in these complicated cases.

7.2. Omphalocele

Omphalocele is a midline abdominal wall defect located at the base of the umbilical cord. The defect is covered by a membranous sac that contains the herniated abdominal contents, and the umbilical cord inserts at the apex of the sac. When the defect is less than 4 cm in size, it is simply referred to as a “hernia of the umbilical cord.” Giant omphalocele refers to larger defects ($>$ 5 cm) that also contain most of the liver. Omphalocele is usually detected by fetal ultrasound during the first or second trimester, with over 90% of cases diagnosed prenatally. A high frequency of fetal aneuploidy, particularly trisomy 18 or 13, is associated with omphalocele [43].

Similar to gastroschisis, the initial management of omphalocele begins with preservation of the sac with sterile saline-soaked gauze or a plastic organ bag, gastric decompression with an orogastric tube, and the administration of intravenous fluids and antibiotics. During the delivery, care must be taken to avoid clamping the umbilical sac, especially in cases of umbilical cord hernia where the small sac can be mistaken for the proximal part of the umbilical cord. Given that approximately half of affected infants have other associated anomalies, a thorough diagnostic workup must be performed to exclude sternal cleft,

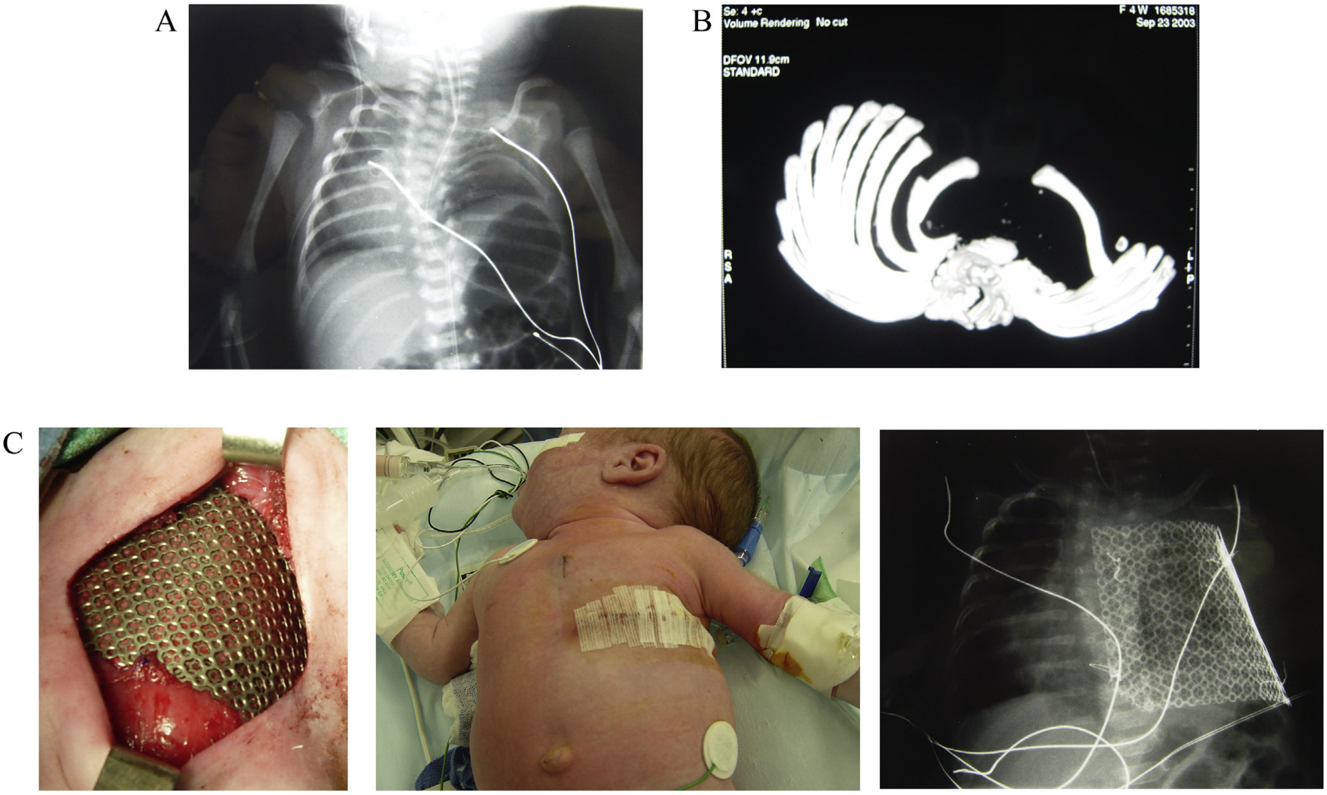

Fig. 7. Premature infant with severe chest wall deformity due to Poland syndrome chest radiograph (A), computed tomography reconstruction (B), and surgical repair using titanium mesh (C). Used with permissions.

ectopia cordis, cardiac defects, diaphragmatic hernia, bladder exstrophy, and cloacal anomalies. With regard to surgical management, small defects can usually be closed primarily within 24–72 h after birth. Larger defects may require delayed closure following the sequential reduction of the herniated organs using a silastic silo over three to seven days. In cases of giant omphalocele, repair of the defect can be achieved by a combination of silastic silo reduction, prosthetic patch closure, and skin grafting or application of topical sclerosing agents (i.e. silver sulfadiazine) to expedite eschar formation with a delayed hernia repair [44].

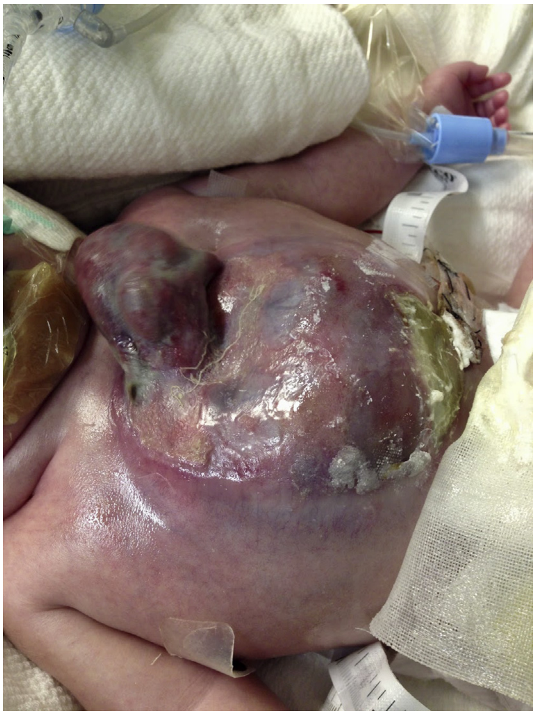

Fig. 8. Premature infant with Pentalogy of Cantrell including omphalocele and ectopia cordis.

8. Conclusions

In summary, critical congenital malformations of the newborn require early detection and prompt intervention to minimize associated morbidity and mortality. In the absence of prenatal detection, the majority of these anomalies present with respiratory distress or obvious external malformations in the early neonatal period. Clinicians must maintain a high index of suspicion for these relatively rare conditions in an effort to quickly secure the correct diagnosis. Ideally, consultation with the pediatric surgeon should occur well before the end of pregnancy when these critical malformations are identified prenatally.

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Declaration of competing interest

None declared.

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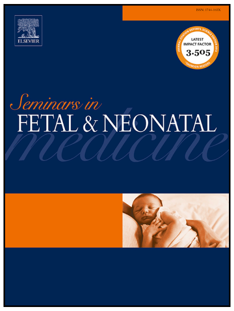

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Neonatal monitoring during delivery room emergencies

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Abstract

Fetal to neonatal transition after birth is a complex, well-coordinated process involving multiple organ systems. Any significant derangement in this process increases the risk of death and other adverse outcomes, underlying the importance of continuous monitoring to promptly detect and correct these derangements by effective resuscitative support. In recent years, there has been increasing efforts to move from subjective and discontinuous monitoring to more objective and continuous monitoring of different physiological parameters. Some of them like pulse oximetry for arterial oxygen saturation and electrocardiography for heart rate monitoring are now part of resuscitation guidelines whereas others like respiratory function monitoring, near infrared spectroscopy, or amplitude integrated electroencephalography are being evaluated.

In this review, we describe some of the physiological parameters that can be monitored during delivery room emergencies and review the evidence for some of the monitoring technologies currently being evaluated.

Keywords:

Neonate; Resuscitation; Monitoring; Respiratory function monitor; Delivery room.

Introduction

Adaptation from fetal to neonatal life at birth is a well-coordinated complex physiological transition involving mainly the cardiovascular and respiratory systems. Amazingly, the majority of infants undergo this transition without much need for assistance and only about 10% of them require some degree of support. This support may vary from application of positive end expiratory pressure (PEEP), positive pressure ventilation (PPV), to chest compression and medications. Effective and timely provision of this assistance is not only critical for survival but also may significantly affect long-term outcome.[1,2]Despite the importance of this critical period, neonatal resuscitation at birth has lagged behind in terms of innovation with most of the interventions performed manually with subjective and episodic monitoring of its effectiveness. This is in stark contrast to infants admitted to the neonatal intensive care unit (NICU) who benefit from continuous and objective monitoring of multiple parameters guiding clinical decision-making.

Over the last decade, there has been significant advances in the field of neonatal resuscitation in the delivery room with continuous monitoring of arterial oxygen saturation (SpO_2) by pulse oximeter, and heart rate using electrocardiography (ECG) being part of the current neonatal resuscitation program (NRP).[3] In addition, there are increasing efforts to evaluate newer technologies including continuous monitoring of ventilation, monitoring of tissue oxygenation and function, and continuous recording of the delivery of resuscitation. (Table) These efforts are not only critical for improving outcomes in individual patients but also for the advancement and quality improvement in the field. In this manuscript, we will discuss some of the evidence and challenges faced by these monitoring strategies.

Monitoring of respiratory function

The most important part of successful transition at birth is aeration of the lungs with the establishment of an air-liquid interface for gas exchange, establishment and maintenance of functional residual capacity, and change from irregular fetal breathing movements to regular inspiratory efforts. The majority of preterm infants and about 3-5% of term infants require support to establish spontaneous ventilation emphasizing the importance of providing adequate respiratory support.

Respiratory function monitor

A respiratory function monitor with a flow sensor interposed between the endotracheal tube or mask and the PPV device can provide a real time display of tidal volume, airway pressures, gas flow and leak during resuscitation.

Tidal Volume

There is ample animal and clinical data suggesting that brief periods of ventilation with excessive tidal volumes at birth can be associated with lung and brain injury.[4-6] The current methods of monitoring the effectiveness of positive pressure ventilation (PPV) are visual estimation of chest rise and improvement in heart rate. The use of chest rise as a marker of appropriate tidal volume has been shown to be often inaccurate. [7,8]

A respiratory function monitor can be used to display tidal volume continuously. Expired tidal volume is a more accurate estimate of volume delivered to the lung due to the larger leaks occurring during inspiration. This data can then be used to adjust peak inspiratory pressure (PIP) or mask position to decrease leak in real time. In a randomized controlled feasibility trial, use of respiratory function monitor during PPV reduced mask leak and the proportion of breaths with excessive tidal volumes.[9,10]

One of the limiting factors for targeting tidal volume during PPV is the limited information on normative values for tidal volume shortly after birth. There is some evidence that spontaneously breathing, relatively mature infants generate tidal volumes between 4-8 ml/kg, but whether this data can be applied to sicker, extremely premature infants is not known.[11,12]

Gas Leaks

PPV using a facemask is the most frequent initial step for resuscitation in the delivery room. Adequate seal around the mask to provide effective PPV is a difficult skill to acquire with gas leaks around the mask resulting in loss of inspiratory tidal volume to the lungs. There is clear evidence that variable amount of leak is common during mask ventilation and this is difficult to estimate clinically.[13,14] This variability of leak during individual breaths increases the risk of insufficient or excessive tidal volume breaths.

The continuous trace of gas flow or tidal volume with the respiratory function monitor provides continuous visual feedback of leaks which can be used to take corrective measures to reduce them. There is evidence from both simulation as well as clinical studies that the use of a respiratory function monitor results in reduced leak during PPV. [9,15]

Other measures of ventilation

All current methods of PPV in the delivery room are prone to high variability in the breath rate and inspiratory time.[16,17] While excessively short inspiratory time may result in delivery of lower than intended tidal volumes, [18] longer inspiratory times when combined with high breath rate may result in less time for expiration resulting in gas trapping. Respiratory function monitor can help decrease these risks by providing numerical values as well as the traces of flow and volume waveforms in real time.

Another use of respiratory function monitor is detection of airway obstruction, which is commonly seen in mask ventilation and is difficult to detect clinically. The use of respiratory function monitoring can help in detecting it earlier so corrective measures can be taken.[19] Similarly, detection of spontaneous breaths with adequate tidal volume can be difficult clinically. Use of a monitor can help to detect spontaneous respiratory efforts and adjust the positive pressure as necessary.

Detection of endotracheal tube position

Endotracheal intubation in the delivery room is a critical step in neonatal resuscitation. It is a difficult skill to acquire and maintain[20] and many infants require a prolonged time or more than one attempt for intubation. Both problems have been associated with worse outcomes.[21-23] The most common methods to confirm correct placement of the endotracheal tube including detection of chest rise and auscultation of breath sounds are subjective and intermittent increasing the risk of a late detection of wrong placement of the endotracheal tube. Colorimetric detection of carbon dioxide (CO_2) in the expired gas is one of the methods commonly used to confirm endotracheal tube placement. This test is dependent on adequate pulmonary blood flow for CO_2 to be exhaled, and may incorrectly suggest tube misplacement .[24]

Observation of the flow curve on a respiratory function monitor can detect correct placement of the endotracheal tube and has been shown to be more accurate as well as quicker in detecting the correct tube position when compared to colorimetric CO_2 detector.[25] In addition, the continuous monitoring data from a respiratory function monitor can be used to detect potential complications such abrupt reduction in tidal volume suggesting misplacement of the tube into a bronchus, or increase in leak suggesting proximal displacement of the tube.

Challenges of respiratory function monitoring

Like many other technologies used in patient care, it is critical that respiratory function monitoring be used with clear evidence of improved clinically relevant outcomes. There is an urgent need for large randomized controlled trials evaluating the use of respiratory function monitor, with some efforts currently underway to accomplish this. Another concern for the use of respiratory function monitoring during neonatal resuscitation is finding a balance between use of the monitoring data and the clinical assessment of the patient to avoid over reliance on the monitor data. There is a need to optimize these monitors for use during neonatal resuscitation making their use simple and reliable.[26,27]

Monitoring of effectiveness of ventilation

The goal of respiratory support is adequate gas exchange with oxygenation and CO_2 removal. In recent years, continuous monitoring of oxygenation with use of oxygen saturation (SpO_2) has become standard of care in neonatal units. In addition, there have been some efforts to evaluate the role of continuous CO_2 monitoring in the delivery room for effectiveness of ventilation.

Monitoring of oxygenation

Oxygen is the most common drug used during neonatal resuscitation after birth. In addition to being required for aerobic metabolism and cellular function, oxygen plays a critical role in pulmonary vasodilatation with increased left ventricular preload and closure of intra – and extra cardiac shunts during fetal to neonatal transition. On the other hand, excessive oxygen supplementation can result in oxidative stress and cellular injury.[28] There is some evidence suggesting that excessive oxygen supplementation during resuscitation is associated with adverse outcomes including higher mortality, thereby stressing the importance for continuous monitoring of oxygenation during this critical period.[29,30]

Pulse oximetry:

Pulse oximetry is the most common method to continuously monitor arterial oxygen saturation (SpO_2) by measuring differential absorption of light at two wavelengths by oxyhemoglobin and reduced hemoglobin. This data has been calibrated against direct measurements of arterial oxygen saturation to provide an accurate value of SpO_2. The advantages of pulse oximetry are ease of use, continuous noninvasive measurement, as well as quite accurate correlation with true arterial oxygen saturation in normoxemic and mildly hypoxemic conditions.

Even though pulse oximetry is the best available tool for monitoring of oxygenation, one should be aware of potential limitations of the technology. One of the limitation is the disagreement between pulse oximetry values and true arterial oxygen saturation with pulse oximetry underestimating arterial oxygen saturations in many situations.[31,32] This limitation is more pronounced in hypoxemic conditions, something which is commonly encountered during transition at birth.[33] In recent years, there has been development of newer pulse oximetry sensors with some improvement in accuracy.[34] Other technological limitations include time delay in signal processing, artifact due to limb movement or low perfusion, all of which limit the accuracy of data when used during resuscitation at birth.

One of the critiques for using SpO_2 for titrating oxygen supplementation is the lack of good quality evidence supporting target SpO_2 ranges during transition. The current target ranges of SpO_2 as advised by NRP are based on healthy neonates with very small number of infants being of extremely low gestational age.[35] In the majority of extremely preterm infants requiring respiratory support, these targets are not easily achieved.[36] There is an urgent need for studies evaluating different ranges of SpO_2 after birth and the effects on clinically relevant outcomes.

Near infrared spectroscopy:

While arterial oxygen saturation is a surrogate of oxygen content in the blood, it does not provide a complete picture of oxygen delivery, which is dependent on multiple factors including cardiac output, hemoglobin content and changes in end organ blood supply. These factors are likely to play a more prominent role at birth during the time of cardiovascular transition with changes in cardiac output and regional blood flow. In addition, tissues also have the ability to increase the extraction of oxygen in the face of decreased oxygen delivery or increased metabolic demand.[37] These factors have led to increasing efforts to evaluate different ways to monitor tissue oxygenation and extraction.

Near infrared spectroscopy (NIRS) is one of the methods to monitor tissue oxygenation by measuring differential absorption of light according to tissue content of deoxygenated and oxygenated hemoglobin to provide oxygen saturation of underlying tissue. Unlike pulse oximetry, NIRS provides a venous weighted saturation of underlying tissue. [38] There has been increasing interest in monitoring cerebral tissue oxygenation ($CrSO_2$) during transition with increasing amount of normative data in neonates.[39] In a small observational study, Baik et al showed an association between IVH and low $CrSO_2$ during transition suggesting the potential utility of $CrSO_2$ monitoring during resuscitation.[40] In a feasibility trial in preterm infants, Pichler et al showed reduction in cerebral hypoxia with use of NIRS guided oxygen supplementation during resuscitation, when compared to controls but there was no significant difference in outcomes. [41] Based on these results, a multicentric randomized trial is currently underway to evaluate NIRS guided oxygen supplementation during resuscitation in preterm infants.[42]

Despite early promising results, many questions still remain regarding use of NIRS during resuscitation. These include variability in values according to the device, limited data on normative values in different gestation age groups, as well as definitive evidence on its effect on outcomes.

Monitoring CO_2 elimination

One of the markers of adequacy of respiratory support during resuscitation is arterial CO_2 levels. Increased CO_2 level not only reflect inadequate ventilation but also may affect cerebral blood flow. One of the methods for CO_2 monitoring is end tidal CO_2 ($ETCO_2$) which uses a CO_2 sensor interposed between the facemask or ET tube and the PPV device. Obtained values have been shown to correlate well with arterial CO_2. [43]

There is limited data on the use of continuous quantitative $ETCO_2$ monitoring during neonatal resuscitation with studies showing feasibility of the method but no effect on proportion of infants with CO_2 outside of a pre-specified range. [44] There is a need for further studies to evaluate the effect on clinical outcome before this technology can be recommended for routine use.

Cardiovascular monitoring

The complex physiologic changes that occur in the cardiovascular system after birth are an integral part of successful fetal to neonatal transition. Establishment of effective ventilation and oxygenation results in a reduction in pulmonary vascular resistance thereby increasing pulmonary blood flow, venous return to the left side of the heart, and an increase in left ventricular output. All these changes are critical for adequate systemic blood flow and any significant perturbation may affect outcome.

Evaluation of heart rate is a critical part of current NRP guidelines, not only as an important marker for the need for resuscitation, but also increase in heart rate is considered as the most reliable indicator of effective ventilation. Despite the importance of accurate heart rate detection, the methods to assess it have been subjective and prone to error until recently. Some of the common methods include palpation of brachial or femoral artery, umbilical cord pulsation, or auscultation of heart rate. All these methods are subjective, provide discontinuous observation, and may interfere with critical components of resuscitation such as ventilation and chest compression. [45]

Pulse oximetry and electrocardiography (ECG) are two methods which have been evaluated the most for continuous noninvasive measurement of heart rate during resuscitation at birth. Since pulse oximetry is dependent on propagation of pulse wave in the artery being monitored, it may provide inaccurate values during conditions of low perfusion, commonly seen during transition after birth. In addition, limitations of pulse oximeter include effect of motion, and the delay in getting accurate data. On the other hand, using pulse oximeter for heart rate detection avoids the need for another monitor or leads placement needed for ECG. The current NRP guidelines recommend ECG as the preferred method for evaluation of heart rate. Both, pulse oximeter and ECG are more reliable and accurate than palpation or auscultation, but there is increasing evidence that ECG may detect heart rate quicker and more accurately than pulse oximeter in certain coditions.[46,47] Some of the rare limitation of using ECG could be in cases of significant subcutaneous edema or pulseless electrical activity with ECG providing inaccurate information underlying the need for not relying on single monitoring technology.[48] Other emerging technologies for heart rate monitoring in the delivery room include doppler ultrasound, auscultation with digital stethoscope, and photoplethysmography.

While heart rate monitoring is commonly used during resuscitation, cardiac output is likely to be a better marker of tissue perfusion. Noninvasive continuous monitoring of cardiac output using electrical velocimetry has been evaluated in the NICU and has been shown to have good correlation with cardiac output measured by echocardiography. There are early reports of its use during transition at birth but further work is needed to validate the technology, generate normative values and learn how this information can be used in clinical management.[49]

Monitoring brain function

The brain is one of the organs at highest risk of injury during resuscitation at birth and there is an increasing effort to monitor its function continuously. While NIRS monitoring provides some information on brain oxygenation and perfusion, amplitude-integrated electroencephalography (aEEG) is a potential tool to continuously monitor cerebral activity during resuscitation. Two recent studies have described the use of aEEG during early transition at birth showing its feasibility and an association between aEEG activity, cerebral oxygenation and the need for resuscitation.[50,51] Advantages of this technology include continuous noninvasive monitoring but some of the limitations are the need for additional equipment and space, motion artefacts, and interpretation of the signal. Significant work needs to be done to define normal and abnormal brain activity during transition, effects of different resuscitation measures, as well as the impact of this type of monitoring on neurological outcomes.

Monitoring effectiveness of resuscitation

All neonatal resuscitation guidelines are based on a set sequence of observations and actions to be performed at set time periods in a highly stressful condition. Currently, there is no mechanism to objectively collect data on deviations from NRP, both in terms of sequence as well as timing. In most conditions, the information is recorded as a summary by the clinical team after the event. This lack of objective monitoring of delivery of resuscitation when combined with the limitations of APGAR scores as marker of infant's condition during resuscitation, makes this critical period of transition at birth relatively inaccessible to critical evaluation. Some of the consequences of this include difficulty in quality improvement, training and advancement of resuscitation providers, developing evidence-based guidelines or objective evaluation of any changes in the guidelines. This is reflected in the current resuscitation guidelines where most of the recommendations are based on no or very limited objective evidence.

One of the methods for monitoring the resuscitation process includes video recording of the procedure. In one such study, Finer et al used video recordings and showed deviation from NRP guidelines in more than half of the cases.[52] Video recording when used in combination with other physiological monitoring data can be used to analyze different steps of resuscitation to analyze specific deficiencies.[53] One of the important deficiencies of current neonatal resuscitation training is reliance on simulation for training which despite significant recent improvements, does not match real life scenarios. Video recording of actual resuscitation can be extremely useful in the training of providers.

Some of the potential challenges for its use includes concerns for privacy for both patient and clinicians, medico-legal issues, as well as the psychological effect on the resuscitation providers. In addition to robust cost benefit evaluation, studies showing positive impact of video recording on clinical outcomes needs to be performed before it can be implemented in routine clinical practice.

Future advances in monitoring in the delivery room

One of the critical components of fetal to neonatal transition at birth is homogenous lung aeration and establishment of functional residual capacity. As opposed to provision of standard respiratory support to all neonates at birth, provision of respiratory support tailored to the specific needs of each infant may potentially results in less lung injury and better outcome. One way to achieve this is by real time monitoring of lung aeration using electrical impedance tomography (EIT) and optimizing the respiratory support accordingly during transition. In one study in preterm lambs, Tingay et al showed that the individualized lung recruitment strategies using EIT may reduce lung injury.[54]

There has been increasing use of closed loop technologies like automated adjustment of inspired oxygen according to measured SpO_2, or adjustment of peak inspiratory pressure according to exhaled and target tidal volume in volume targeted ventilation in the neonatal intensive care unit. The next step for continuous monitoring in the field of neonatal resuscitation is evaluation of these technologies. Before these new systems can be used clinically, there is a need to develop evidence based normative ranges for these measures and interventions at different stages of transition along with critical evaluation of their impact on clinically relevant outcomes.

As neonatal resuscitation at birth becomes more complex and requires highly skilled clinicians, provision of these services on every birth is a great challenge not only in developing countries but also in the more advanced settings. As the majority of infants do not require much support at birth, low volume and unpredictability of the need for neonatal resuscitation makes availability of skilled personnel and retention of their skills very challenging. One of the potential ways to overcome this challenge is the use of telemedicine with both simulation training of the staff as well as real time support during resuscitation.[55,56]

One of the advantages of monitoring neonatal resuscitation is the collection of various parameters of oxygenation and ventilation along with the degree and timing of support provided during fetal to neonatal transition. If these data are collected in a large number of infants of different gestational ages, and requiring different respiratory support and correlated with clinical outcomes, these can not only be used to develop evidence-based guidelines but also can be used to develop automated systems with machine learning capabilities. In addition, these data can be used in combination with cellular and molecular markers of tissue injury to understand the pathways of various perinatal disease processes and develop newer treatment strategies.

Conclusion

The transition from a placenta dependent fetus to a self-sustained neonate after birth is a complex process requiring aeration of lungs, improving oxygenation with resultant cardiovascular changes. A minority of infants need support during this transition but when needed, timing and effectiveness of these efforts are not only lifesaving but also may have long-term benefits. There are concerted efforts to objectively evaluate the effects of support during this transition. So far, most of the currently recommended monitoring strategies are simple technologies routinely used in NICU, like pulse oximetry for SpO_2 or ECG for heart rate monitoring.

There is increasing interest in bringing other technologies currently used in NICU, like ventilation parameter monitoring with RFM, or monitoring of brain oxygenation with NIRS to the delivery room. Some of the obstacles for using these or any other monitoring technology in the delivery room include the lack of normative values, cost and space limitations, as well as limited information on their impact on the patients and on the clinical team. There is a need for well conducted large randomized controlled trials evaluating relevant outcomes before any of these monitoring strategies can be recommended for routine use.

As in other fields of medicine, increasing use of objective, continuous monitoring is likely to become an integral part of neonatal resuscitation at birth. Whether these changes will improve long term health will need to be closely evaluated.

Practice points

- Pulse oximetry for arterial oxygen saturation and ECG for heart rate detection are more accurate than subjective assessment, but their impact on clinical outcome is not known.
- Respiratory function monitoring has been shown to reduce mask leak and decrease high tidal volumes with studies on their impact on clinical outcomes currently underway.
- There is limited normative data for infants of different gestational ages for currently used monitoring parameters in the delivery room.

Research directions

- Role of tissue oxygenation monitoring after birth and its effect on clinical outcomes.
- Use of respiratory function monitor data to adjust respiratory support and its impact on clinical outcomes.
- Development of tools for continuous monitoring of regional perfusion and effect of different management strategies on outcomes.

Figure 1: Representative tracing of flow, pressure and volume during PPV with mask ventilation. Darker vertical line represent start and end of inspiration and lighter vertical lines represent time. There is both inspiratory and expiratory leak with flow above the baseline. There is no inspiratory or expiratory leak flow in last two positive pressure breaths suggesting mask repositioning.

Figure 2: Representative tracing of flow, pressure and volume during PPV. Darker vertical line represent start and end of inspiration and lighter vertical lines represent time. There is considerable variability in variability in inspiratory time and breath rate.

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Table: Neonatal monitoring technologies during delivery room emergencies

Monitoring technology	Potential role during delivery room emergencies	Current Evidence
Respiratory function monitor	• Tidal volume monitoring and targeting. • Monitoring of breath rate, inspiratory time, and PEEP. • Detection of gas leak around the face mask. • Assessment of endotracheal tube placement. • Detection of spontaneous breathing effort.	• Two small studies showed reduction in mask leak, intubation rates, oxygen supplementation, and number of breaths with excessive tidal volume. [9,10] • No current evidence on longer term outcomes.
Quantitative CO_2 monitoring	• Avoidance of extremes of CO_2 during resuscitation and transport	• Multiple studies reported the feasibility of quantitative CO2 monitoring during resuscitation but no effect on incidence of

		hypo or hypercarbia or other clinical outcomes.
Pulse oximetry	- Titration of oxygen supplementation to target arterial oxygen saturation. - Monitoring of arterial pulse wave as a surrogate for heart rate.	- No RCTs evaluating the effect of pulse oximetry during neonatal resuscitation at birth on clinical outcomes. - Some evidence that pulse oximetry could be less reliable and slower to detect heart rate when compared to ECG - No evidence of impact on clinical outcomes.
Near infra-red Spectroscopy	- Monitoring of tissue specific oxygenation with titration of oxygen supplementation to the desired targets.	- Pilot feasibility RCT enrolling 30 preterm infants showed reduction in low cerebral oxygen saturation with use of NIRS to guide respiratory support at birth with no impact on clinical outcomes.[41]
Electrocardiography	- Monitoring of heart rate.	- Gold standard for heart rate assessment in

		newborn infants at birth. No evidence of impact on clinical outcomes.
Electrical velocimetry	• Monitoring of cardiac output during resuscitation.	• Prospective observational study showed feasibility of the technology. No current evidence of impact on outcomes.
Amplitude integrated EEG	• Monitoring of electrical activity of brain during resuscitation.	• Prospective observational study showed feasibility of the technology. No current evidence of impact on outcomes.
Video recording of resuscitation	• Auditing and quality improvement in delivery room practices. • Detection and correction of specific deficiencies in the provision of resuscitation. • Real time guidance and support during resuscitation.	• No current evidence of impact on clinical outcomes.

Figure 1

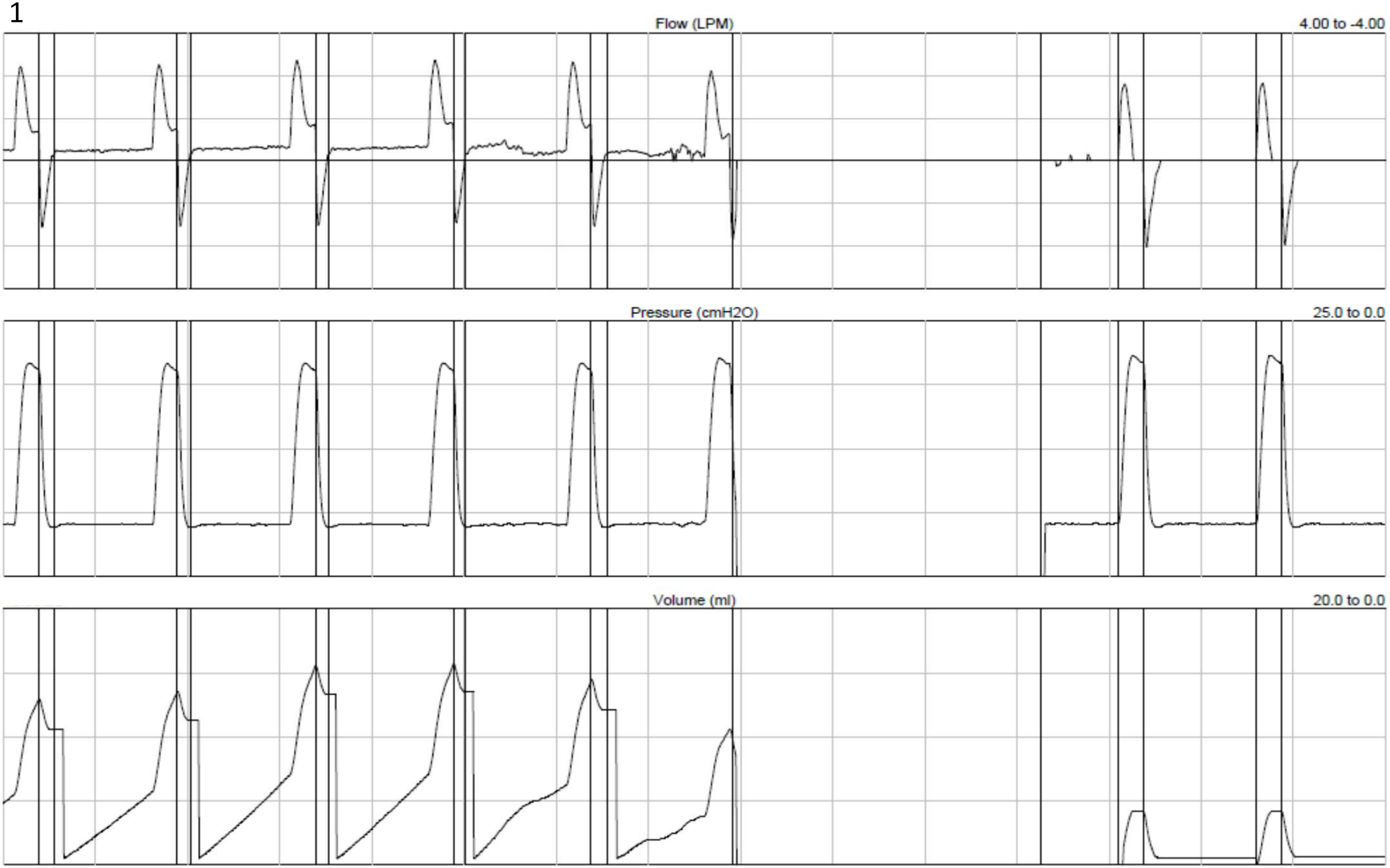
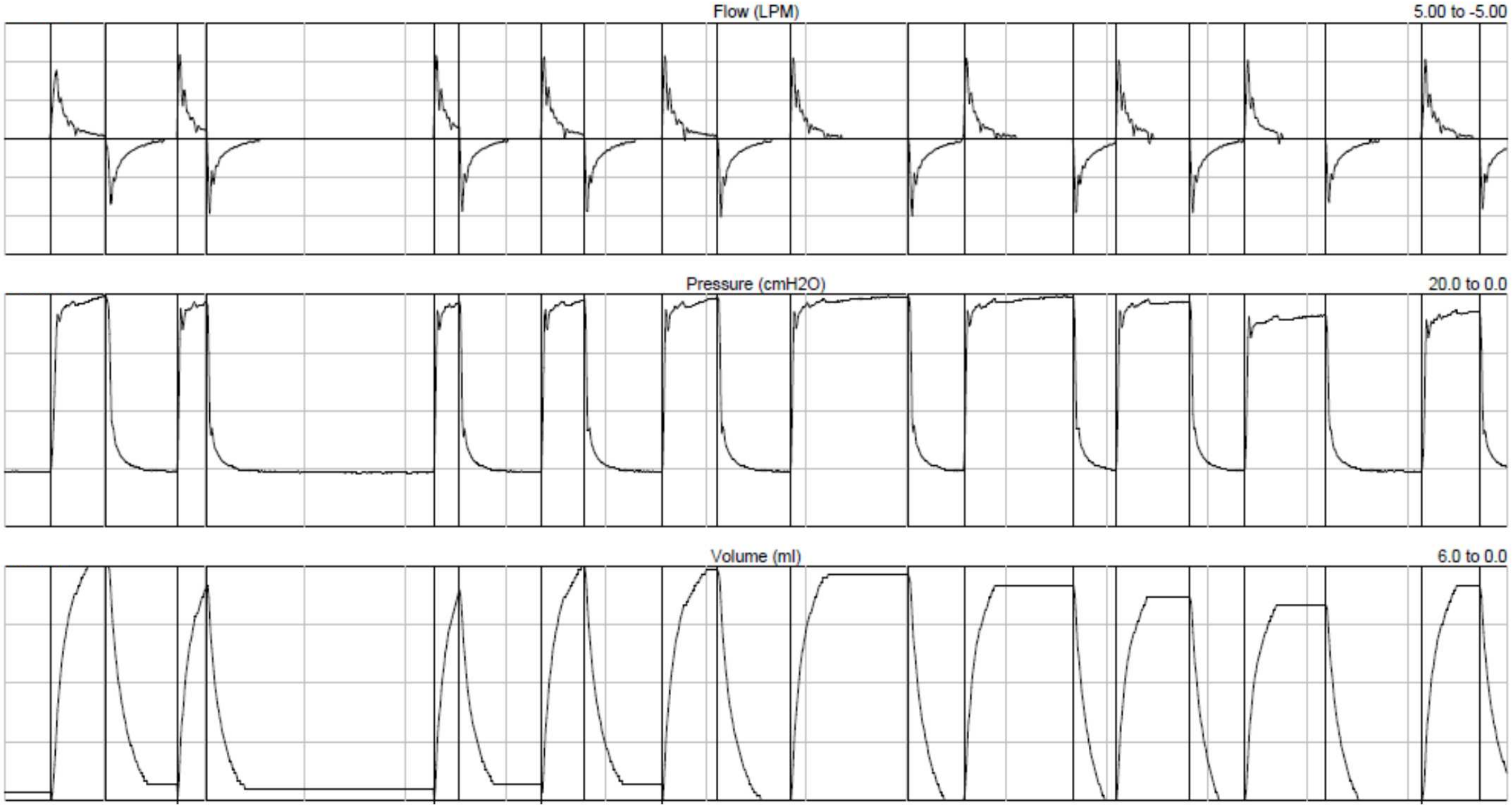

Flow (LPM)
4.00 to -4.00
Pressure (cmH2O)
25.0 to 0.0
Volume (ml)
20.0 to 0.0

Figure 2



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Drugs in the delivery room

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ABSTRACT

The need for cardiopulmonary resuscitation in newborns is quite rare, as most non-vigorous infants respond well to effective ventilation. For the minority of babies who do not respond to adequate ventilation, chest compressions are necessary using the preferred two thumb technique. Since effective ventilation remains a key component to successful resuscitation, chest compressions are coordinated with ventilations in a 3:1 ratio. If despite adequate ventilation and compressions, the heart rate remains below 60 beats per minute, epinephrine is indicated. The intravenous route is preferred over the endotracheal route and the recommended dose of epinephrine is 0.01–0.03 mg/kg. This can be repeated every 3–5 min until return of spontaneous circulation is achieved. In rare instances, when there is no response to these above measures and in infants who show evidence of significant hypovolemia, volume replacement should be considered.

The vast majority of newborn infants make the transition from fetal to neonatal life without needing intervention beyond supportive measures of providing warmth and stimulation. However, an estimated 10% of neonates do require some help, which mostly takes the form of establishing effective ventilation [1]. Fortunately, the need for cardiopulmonary resuscitation (CPR) with or without the administration of medications is quite rare (approximately 1.2 per 1000 live births) [2]. When this happens however, it is often due to fetal asphyxia in the intrapartum period and has high rates of morbidity and mortality [2,3].

1. Chest compressions

Current Neonatal Resuscitation Program (NRP) guidelines recommend chest compressions for infants who do not respond to effective ventilation and continue to have a heart rate less than 60 beats per minute (bpm) despite at least 30 s of positive pressure ventilation that results in lung inflation. These infants are likely to be asphyxiated and have significant acidosis with consequent myocardial depression. This results in an inability of the heart to adequately pump blood to the lungs and other vital organs. Therefore, there is need to mechanically compress the chest to pump blood to the lungs, brain and heart as well as other vital organs, while simultaneously continuing to ventilate the lungs until the myocardium is oxygenated enough to restore spontaneous function [4].

Given the importance of simultaneously continuing positive pressure ventilation while doing chest compressions, it is preferred that chest compressions be administered from the head of the bed, using the two thumb technique [4]. This allows the compressor to have unrestricted access to the chest and enables proper positioning of the hands in an ergonomically stable manner. Additionally, this position also allows other team members to have room to gain umbilical venous access in the event that medication administration becomes necessary (Fig. 1). Given the importance of ventilation in the return of spontaneous circulation (ROSC), it is essential to coordinate chest compressions with ventilation. While the optimal compression to ventilation ratio for the resuscitation of an asphyxiated newborn has yet to be established [5], current NRP guidelines state that the compression rate should be 90 compressions per minute coordinated with 30 ventilations per minute for a total of 120 events per minute. This is delivered by 3 compressions followed by 1 ventilation every 2 s [4].

2. Epinephrine

Despite adequate ventilation of the lungs and supplementing cardiac output with chest compressions, a small minority of babies (approximately 0.001–0.003% of term and late preterm births) may still have a heart rate below 60 bpm [4]. These newborns may benefit from the use of medications and in some rare instances, volume expansion, given in conjunction with synchronized ventilations and chest compressions.

Epinephrine is the only medication recommended by the International Liaison Committee on Resuscitation for use in newborn resuscitation. It is an endogenous catecholamine with high affinity for α1, β1 and β2 receptors present in cardiac and vascular smooth muscle

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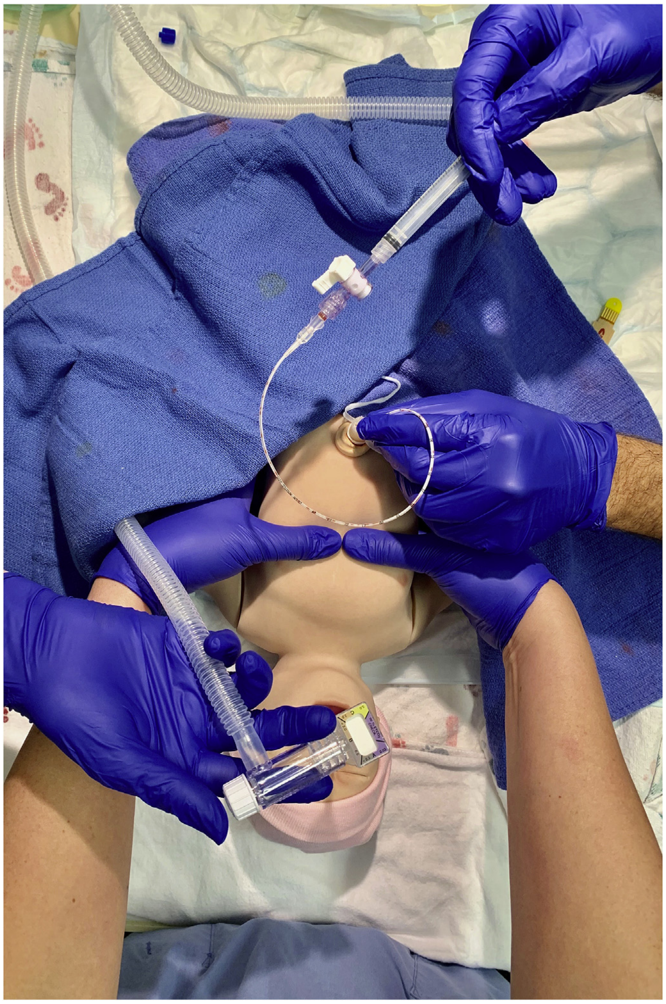

Fig. 1. Team positioning around warmer during extended resuscitation. Note the space available to obtain umbilical venous access while ventilation and head of bed chest compressions are being performed.

[6]. Increased heart rate, conduction velocity and contractility are mediated by its action on β1 and β2 receptors, the sinoatrial node (SA) and the atrioventricular (AV) node. Additionally, through its α1 mediated action, it can affect peripheral vascular resistance by causing peripheral vasoconstriction [7]. In fact, in a canine model of asphyxia, Otto et al. demonstrated no ROSC in canines treated with phenoxybenzamine, a pure α blocker, while there was a 75% rate of ROSC in animals who received the β blocker propranolol [8]. These findings strongly suggest that the efficacy of epinephrine in resumption of spontaneous circulation from asphyxia cardiac arrest is primarily due to α adrenergic receptor stimulation.

In severely asphyxiated newborns, bradycardia and/or cardiac arrests frequently occur as a consequence of underlying hypoxemia, hypercarbia and metabolic acidosis. These infants are commonly very vasodilated with low systemic vascular resistance, which translates into a low aortic diastolic blood pressure (ADBP). Since the coronary perfusion pressure (CPP) is dependent on the ADBP, this can result in insufficient coronary blood flow. Given the α1 mediated effects of epinephrine, it is possible that epinephrine use in these newborns would increase peripheral vascular resistance, thus increasing the CPP and improving coronary blood flow. Interestingly, this theory has not been proven true in a lamb model of neonatal asphyxia, in which epinephrine failed to significantly improve the heart rate, cardiac output and blood pressures in asphyxiated, acidotic lambs [9], creating some controversy regarding this theory.

Table 1
Unique characteristics of transitioning neonatal physiology which affect epinephrine absorption.

1. Fluid filled alveoli which dilute epinephrine
2. High pulmonary vascular resistance may limit pulmonary blood flow
3. Presence of patent ductus arterious (PDA) and patent foramen ovale (PFO), in the presence of high pulmonary pressures may potentiate right-to-left cardiac shunts, enabling blood to bypass the pulmonary circulation
4. Pulmonary vasoconstriction from profound mixed metabolic and respiratory acidosis from asphyxia

As discussed earlier, the causes of bradycardia and ultimately cardiac arrest in newborns differ significantly from the etiologies of adult cardiac arrest, which is commonly characterized by the abrupt cessation of cardiac output following arrhythmias. Adult cardiac arrest usually occurs in a setting of adequately oxygenated blood. Due to the rarity of requirement for medications in neonatal resuscitation, large clinical trials are lacking and current recommendations regarding timing, route and dosing of epinephrine are based largely on animal models or pediatric or adult studies which do not sufficiently reflect the unique features of the transitioning newborn cardiorespiratory system [10] outlined in Table 1.

Prior to any discussion regarding the best route of dosing, it is important to have a basic understanding of the pharmacokinetics of epinephrine. Adult animal data comparing different routes of epinephrine administration in a swine model of traumatic cardiac arrest demonstrated that while the intravenous (IV) route resulted in a higher maximum concentration, the endotracheal (ET) route resulted in variable absorption as compared to the intravenous and intraosseous (IO) routes. However, in this study, the time to ROSC was not substantially different between the three routes employed [11]. While the absorption of endotracheal epinephrine in adult swine was shown to be variable, the bioavailability of ET epinephrine in transitioning neonatal animal models would theoretically be further diminished due to the administration of the ET epinephrine into fluid filled lungs which might additionally hamper absorption into the blood stream. This was elegantly shown in a recent study by Nair et al. in which the investigators compared peak plasma concentrations after ET epinephrine administration in two groups; one group consisting of term transitioning asphyxiated newborn lambs and the other comprising postnatal, post transitioned asphyxiated lambs. They demonstrated lower peak plasma concentrations in the transitioning newborns as compared to the postnatal lambs [12].

Moreover, in a transitioning lamb model of neonatal asphyxia, Vali et al. [13] compared median time to ROSC and peak plasma concentrations between ET doses of epinephrine (0.1 mg/kg) and lower IV and direct right atrial (RA) doses of epinephrine (0.03 mg/kg). The median time to achieve ROSC was significantly longer in the ET epinephrine group as compared to the IV and RA epinephrine groups. That, coupled with the finding of lower peak plasma epinephrine levels in the former group additionally contributes to evidence that ET epinephrine is less efficacious than IV epinephrine.

The superior efficacy of IV epinephrine over ET epinephrine is further established by a retrospective clinical review of all neonates requiring at least one dose of ET epinephrine in the delivery room. It was shown that while 32% of these patients achieved ROSC in response to the first dose of ET epinephrine, of the remaining who failed the initial ET dose, 77% achieved ROSC after IV administration of the drug [1]. It was thus concluded that ET epinephrine is often ineffective. However, in this retrospective study, the dose of ET epinephrine studied was 0.01mg/kg-0.03 mg/kg, which is similar to the IV dose. Given the knowledge derived from animal data with respect to the decreased absorption of ET epinephrine from the fluid filled lungs, this conclusion is unsurprising. Data from some animal studies suggests that higher doses of ET epinephrine (0.05–0.1 mg/kg) may have better potency [14,15]. But the caveat to this is that these animal studies were all performed in post transitional animals which do not feature all the unique aspects of neonatal transitional physiology that have been discussed previously. Indeed, another recent retrospective clinical study examined the efficacy of higher dose ET epinephrine (0.03 mg/kg to 0.05 mg/kg) as compared to IV epinephrine and demonstrated that both doses of epinephrine when administered via the ET tube often failed to achieve ROSC without subsequent IV epinephrine administration. This could possibly be explained by those factors reviewed in Table 1 which limit the absorption and distribution of the drug [10].

In light of the robust evidence supporting the superiority of the IV route of epinephrine over the ET route, current guidelines strongly recommend establishing IV access and administering IV epinephrine if indicated. In the delivery room, IV access is readily obtained by placing a low lying umbilical venous catheter (UVC). The catheter is inserted between 3 – 5 cm and adequate positioning can be ascertained by obtaining blood return. In the event that IV access is unattainable, it is feasible to attempt IO access considering that there is evidence that the pharmacokinetics of IO and IV epinephrine are comparable [11]. Moreover, a simulation study comparing IO and umbilical catheter placement demonstrated faster IO placement without any difference in technical errors or perceived ease of use [16], suggesting that this may be a good option for inexperienced healthcare professionals attending deliveries. While IV/IO access is being established, it is reasonable to consider a dose of ET epinephrine at 0.05mg/kg-0.1 mg/kg using the 1:10,000 (0.1 mg/ml) preparation [4].

Although IV epinephrine unequivocally has better bioavailability than ET epinephrine, the ideal dose to achieve ROSC while minimizing side effects is as yet uncertain. Since the bioavailability of IV administered epinephrine is 100%, it is plausible that a lower dose may be sufficient to achieve ROSC. This is borne out by animal data which suggests that using higher doses of epinephrine can be detrimental. In an ovine model of asphyxia, Burchfield and colleagues administered graded doses of epinephrine ranging from 0.001mg/kg-0.1 mg/kg. They demonstrated that stroke volume and cardiac output were blunted in those animals administered the high dose of epinephrine (0.1 mg/kg) [17]. Moreover, other animal data demonstrate trends towards decreased cerebral blood flow and higher post resuscitation mortality with high dose epinephrine of 0.2 mg/kg as compared to 0.02 mg/kg [18,19]. Indeed, there is also pediatric clinical data available that furthers the notion that low dose epinephrine (0.01 mg/kg) is equivalent in achieving ROSC as compared to high dose epinephrine (0.1 mg/kg) [20]. Similar findings were demonstrated in another pediatric prospective randomized controlled trial (RCT) conducted by Perondi and colleagues. They found a concerning trend towards increased mortality in the post-resuscitative period, with fewer patients assigned to receive high dose epinephrine (0.1 mg/kg) surviving to hospital discharge [21]. Given all these data evidencing equivalence in the rates of ROSC, coupled with the concerning negative effects associated with high dose epinephrine, current NRP recommendations support the use of lower doses of IV epinephrine in the range of 0.01–0.03 mg/kg. This can be repeated every 3–5 min until ROSC is achieved [4].

3. Practice points

- Epinephrine is indicated if the baby's heart rate remains below 60 bpm despite at least 30 s of effective PPV, preferably through an advanced airway AND

- Another 60 s of chest compressions coordinated with PPV using 100% oxygen.
- IV route is highly recommended over the ET route. Umbilical venous access is preferred. If IV access is unattainable, IO access can be considered.
- While awaiting IV/IO access for administration of epinephrine, it is reasonable to consider an ET dose of epinephrine in the range of 0.05–0.1 mg/kg using the 1:10,000 concentration.
- IV epinephrine dose ranges from 0.01 to 0.03 mg/kg. There is currently no evidence supporting the use of higher IV epinephrine doses.
- The IV dose can be repeated every 3–5 min until ROSC is achieved.

4. Future research directions

Since it is important to minimize interruptions in chest compressions to optimize coronary perfusion pressure and aid ROSC, it is worth investigating the role quantitative end tidal CO2 (ETCO2) monitoring may play during resuscitation. There are three determinants of ETCO2: CO2 production, alveolar ventilation and pulmonary perfusion. Thus, if CO2 production and ventilation are constant, pulmonary perfusion would determine the amount of exhaled CO2 [22]. Since pulmonary perfusion is dependent on cardiac output, it stands to reason that an increase in the amount of ETCO2 would correlate with increased cardiac output and could be used as a surrogate measure of ROSC. This theory has been demonstrated in adults [23]; however it wasn't until very recently that Stine et al., in a retrospective cohort study of resuscitated infants in the pediatric intensive care unit (PICU) and pediatric cardiovascular intensive care unit (CVICU), demonstrated similar findings in an infant age group [22]. Further studies are necessary, not only to corroborate this evidence, but also to evaluate the use of ETCO2 in the delivery room.

5. Volume resuscitation

While effective ventilation is a key step in any resuscitative attempt, adequate circulating volume is another important condition that needs to be fulfilled for successful achievement of ROSC. The need for volume resuscitation in the delivery room is quite rare but has the potential to be lifesaving under certain circumstances. Determining which babies would benefit from volume resuscitation is an important part of the decision making process during an extended resuscitation. Giving additional volume to euvolemic infants in a last ditch effort to improve the heart rate comes with inherent risks, as evidenced by piglet studies, which demonstrated that the use of volume expanders was associated with the development of pulmonary edema without any significant increase in BP [24]. Moreover, there is also evidence that rapid volume administration can impact the coagulation profile, decreasing clot strength [25]. Teams resuscitating preterm infants should be cognizant of the risk of intracranial hemorrhage with rapid volume administration. For these reasons, it is critical to restrict volume administration to those infants who are deemed to be hypovolemic. In instances where there has been evidence of blood loss (Table 2), it is reasonable to assume that these babies may be hypovolemic and candidates to benefit from volume expansion, especially in the presence of signs of shock such as pallor, delayed cap refill and weak pulses [4]. Thus, administration of a volume expander is indicated if the baby does not respond to previous optimized steps of resuscitation AND there is evidence of hypovolemia.

If blood loss or severe fetal anemia is suspected, emergency, noncross matched, type O, Rh negative packed red cells (PRBC) is the fluid of choice for blood loss replacement since it is critical to re-establish oxygen delivery to tissues. The initial recommended dose for any initial volume expansion is 10 ml/kg [4] , given via the umbilical vein or via

Table 2
Indications for volume resuscitation in the delivery room.

1. Acute fetal-maternal hemorrhage
2. Bleeding vasa previa
3. Extensive vaginal bleeding
4. Placental laceration
5. Abruption due to shearing forces, such as a high speed motor vehicular accident
6. Fetal trauma
7. Umbilical cord blood loss

the IO route if IV access is unavailable. Although no clinical trials are available, current guidelines recommend infusing this volume over 5–10 min.

In the event of non availability of O negative PRBC, or if availability will take time, it is reasonable to use an alternative volume expander in the interim period. Evidence shows similar efficacy of crystalloid and colloid solutions [26], however, crystalloids such as 0.9% Saline are generally preferred as they are readily available, cheaper and carry a lower risk of infection [27,28].

6. Sodium bicarbonate

Despite a long history of widespread use, objective evidence that administration of sodium bicarbonate improves outcomes for patients with cardiopulmonary arrest or metabolic acidosis is lacking [29]. In fact, there is concern that use of sodium bicarbonate may compromise coronary perfusion pressure by reducing systemic vascular resistance, producing hypernatremia, hyperosmolarity and excess carbon dioxide, exacerbating central venous acidosis; all potentially contributing towards increased mortality rates [29]. Given these concerns, coupled with the absence of concrete data showing any benefit of use, sodium bicarbonate is NOT recommended for routine use in the delivery room.

7. Naloxone

Naloxone, a specific opiate antagonist, has historically been used in the management of respiratory depression in neonates who may be exposed in utero to opiates. However, a Cochrane meta-analysis of all available relevant clinical trials revealed that although there is some evidence that naloxone may increase alveolar ventilation, there is no strong evidence that naloxone confers any clinically important benefits to newborn infants with respiratory depression [30]. Hence, the current recommendations do NOT support use of naloxone in the delivery room with the preference being to concentrate on providing adequate and effective respiratory support.

In rare but tragic instances, despite optimizing resuscitative measures, the newborn may not respond and remain with an undetectable heart rate. After confirming that the advanced airway continues to remain in place with good chest movement and adequate chest compressions are being administered, ensure that appropriate dosages of epinephrine are being given and there is no evidence of a pneumothorax. If all these conditions are met, NRP guidelines state that absence of a detectable heart rate at 10 minutes is a strong predictor of mortality [4]. It may be reasonable to consider discontinuation of resuscitative measures at this time, but that decision may be dependent on several factors, including but not limited to, gestational age and the family's previously expressed feelings regarding acceptance of morbidity [4]. Hence, these decisions should be made on a case by case basis.

Conflicts of interest

The authors do not have any conflicts of interest.

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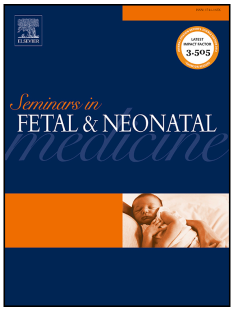

Dealing with Neonatal Emergencies in Low-resource Settings

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Dealing with Neonatal Emergencies in Low-resource Settings

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Synopsis

We describe the development and delivery of neonatal care including trends and impacts of major interventions on neonatal mortality particularly in low-resource settings. Low- and middle-income countries continue to be major contributors to neonatal mortality. Although there has been progress in reducing neonatal mortality, neonatal deaths are contributing an increasing percentage of childhood mortality. Several interventions targeting neonatal care such as neonatal resuscitation and essential newborn care have contributed to improved outcomes. However, there are still many neonatal deaths that are preventable with known effective interventions. This review addresses interventions proven effective in reducing neonatal mortality, challenges to implement them, and future directions of implementing these interventions in low- and middle-income countries.

Keywords:

Resuscitation

Countries, developing

Neonatal Mortality/ history

Neonatal Mortality/ trends

Neonatal Mortality/ epidemiology

Neonatal Mortality/ therapy

Key Points

1. Low- and middle-income countries have disproportionately high numbers of neonatal mortality and morbidity.

2. Several low-cost and high-impact interventions delivered as packages have shown to improve neonatal outcomes in low and middle-income countries.

3. There continues to be a large unmet need for quality newborn care, especially soon after birth and the first few days after birth. Unless this gap in healthcare provision is addressed, deaths from preventable causes and serious morbidities will continue to burden families and society in low-resource settings.

History of Global Neonatal Mortality and Morbidity

Childhood mortality approached 50% in the 18th and 19th century in some countries in Europe [1]. Advances in medicine and recognition of child and newborn mortality as a problem led to a gradual decline in child and newborn mortality in developed countries in the early 20th century [2]. Earlier data on neonatal mortality are incomplete, and comprehensive data on global neonatal mortality including data trends from different countries are available only since 1990 [1, 3]. Neonatal mortality rates have been improving during the last few decades, but the rate of decrease has been slower as compared to the decline in under 5 mortality [4, 5]. Therefore, the proportion of neonatal mortality to under 5 mortality has increased to 45% [6, 7].

Chronology of Neonatal Resuscitation

The earliest account of neonatal resuscitation was described in texts dating back to 6th century BC [8, 9]. Resuscitation as an intervention that could save lives was identified only in the late 18th century, beginning the era of formalized resuscitation training and certification [9]. This led to the formation of various societies focused on resuscitation guidelines [10]. One of the first efforts directed at formal neonatal resuscitation training was in mid-1970s and was called Neonatal Educational Program [11]. In 1987, the American Academy of Pediatrics developed the Neonatal Resuscitation Program (NRP) [11]. By 1989, the program was adopted across North America, and early international dissemination began [12]. This was followed by a rapid global adoption period in which many hospitals and teaching institutes across the world implemented neonatal resuscitation program [13]. In 1992, the International Liaison Committee on Resuscitation (ILCOR) began an international collaborative effort to form an international consensus on resuscitation including neonatal resuscitation [14]. Evidence-based neonatal resuscitation guidelines began to be formulated every 5 years with the most recent one in 2015 [15, 16]. There has been a universal uptake of NRP and subsequent improvement in neonatal resuscitation practice and outcomes in high-income countries [12].

Challenges to Neonatal Resuscitation in Low- and Middle Income Countries

Approximately 98% of all perinatal and neonatal deaths occur in low- and middle-income countries [17]. Neonatal mortality is about 50 times higher in low- and middle-income countries compared to high-income countries [18]. Although global under 5 mortality has decreased substantially, the decrease in neonatal mortality has been more modest [19]. Failure to initiate spontaneous breathing is a major cause of perinatal mortality and morbidity [20-22]. Approximately 13 million neonates require resuscitation [18] and of them, 3-6 million neonates require assistance to initiate respirations [23]. Neonates who require respiratory support, if not assisted promptly, decompensate rapidly resulting in death [24]. Delivery of prompt and effective neonatal resuscitation is the only intervention that could potentially prevent mortality in such scenarios [25-32]. In an observational study, 94% of neonates requiring resuscitation responded to basic steps like suctioning and bag and mask ventilation; delay in the administration of basic resuscitation was associated with the corresponding rise in the risk of death [33].

Low- and middle-income countries continue to have high neonatal mortality secondary to high rates of home births with lack of trained birth attendants as well as lack of prompt and effective basic neonatal resuscitation facilities [18, 34, 35]. About 60 million births/year happen outside birthing facilities mainly at home or the birth attendants' homes. Rates of home births are as high as 50-90% in some countries [18, 36]. In the 60 million births that occur outside of birthing facilities, close to 52 million deliveries occur without a trained birth attendant [37, 38]. Additionally, health care facilities are ill-equipped, and many of them lack trained neonatal resuscitation providers [18]. In a survey from 6 African countries, only 2%–12% of birthing hospitals had trained neonatal resuscitation providers and only 8%–22% of the facilities had neonatal resuscitation equipment [39].

NRP and ILCOR guidelines were based on clinical research mostly originating from developed countries [40]. As NRP and ILCOR guidelines were based on best scientific evidence and did not consider resource and personnel constraints, application of AAP and ILCOR neonatal resuscitation guidelines was constrained in resource-limited settings from low- and middle-income countries [18].

Resuscitation Guidelines for Low- and Middle-income Countries

Neonatal resuscitation was assumed to require expertise and resources available only in neonatal intensive care units [13, 41]. Soon after the implementation of NRP, growing evidence suggested that most of the neonates who required resuscitation could be saved by simple interventions such as drying, stimulation, and bag and mask ventilation [39, 42-44]. Due to the constraints in implementation of NRP/ ILCOR guidelines in resource-limited settings and the evidence suggesting that most of the neonates who require resuscitation can be saved by simple interventions, World Health Organization (WHO) initiated training and implementation of Essential Newborn Care (ENC) in 1994 [45] which also included basic neonatal resuscitation.

Focused Basic Newborn Resuscitation guidelines were issued by WHO in 1998 [46]. These guidelines were revised by WHO in 2012 in the publication Basic Neonatal Resuscitation [47] and Early Essential Newborn Care (EENC) guidelines in 2014 [48]. In 2006, the American Academy of Pediatrics constituted a global implementation task force to develop a simulation-based training package for neonatal resuscitation for low- and middle-income countries [49]. AAP together with partners including WHO, the US Agency for International Development, Save the Children's Saving Newborn Lives program, the National Institute of Child Health and Human Development, and the Laerdal Global Health Group introduced neonatal resuscitation guidelines for low- and middle-income countries named Helping Babies Breathe (HBB) in 2010 [13] which was revised in 2016 [50]. AAP has also issued general newborn care guidelines for low- and middle-income countries called Essential Care for Every Baby (ECEB) in 2014 [51] and Essential Care for Small Babies (ECSB) in 2015 [52]. A summary of the guidelines covered in these educational programs is included in Table 1.

Evidence of the Impact of Neonatal Resuscitation Programs in Low- and Middle-income Countries

Although there have been several large trials for assessing the effectiveness of basic resuscitation in low- and middle-income countries, most of the research has been observational or quasi-randomized due to the ethical challenges associated with an obviously life-saving intervention such as neonatal resuscitation.

In an interventional multicenter trial (N=71,689 neonates), early neonatal (< 7 day) mortality decreased from 36.6/1000 to 25.1/1000 live births following ENC training of midwives in health clinics ($p<0.001$) and to 15.9/1000 live births following NRP training [28]. A large multi-country study with active baseline before and after study and cluster randomized controlled design (First Breath Trial) (N=120,009 births, birthweight >1500 grams) assessed the impact of essential newborn care and basic neonatal resuscitation training in rural community birth attendants of six countries (Argentina, Democratic Republic of Congo, Guatemala, India, Pakistan, and Zambia) [25]. ENC implementation resulted in a significant decrease in the stillbirth rate (RR 0.69; CI 0.54, 0.88; $p<0.01$) and perinatal mortality. However, after ENC training, NRP training was not associated with a significant reduction in neonatal mortality or stillbirth rate in clusters that were randomized to NRP training compared to control clusters. The findings of this trial indicate that neonates who were stillborn before ENC training were surviving due to the provision of basic resuscitation. Additional NRP training after ENC training was not associated with significant improvement in perinatal/neonatal mortality suggesting that ENC was equally effective to NRP in these low-resource settings [25]. Similar to ENC training trials, large multicenter trials of training birth attendants from low- and middle-income countries in Helping Babies Breathe (HBB) have shown to significantly decrease stillbirth rate and neonatal mortality [30, 53, 54]. The systematic review and meta-analysis of interventional trials of basic neonatal resuscitation training of birth attendants from low- and middle-income countries has shown a significant decrease in the incidence of fresh stillbirth (RR 0.74, CI 0.61 to 0.90), perinatal mortality (RR 0.82, 95% CI 0.74 to 0.91), and neonatal mortality (RR 0.58, 95% CI 0.42 to 0.82) [55]. The reduction is stillbirth from a postnatal intervention indicates that resuscitation can be effective even when there are no signs of being alive at birth.

Neonatal Emergencies in Low-resource Settings

As per recent estimates, there are close to 3 million neonatal deaths per year with the overwhelming majority of them (~98%) happening in low- and middle-income countries [6, 7]. Leading causes of neonatal mortality include prematurity (29-35% of neonatal deaths), birth asphyxia or intrapartum-related events (23%), sepsis (21-36%) and congenital anomalies (11.3%) [7, 56]. It should be noted that assignment of a single cause of neonatal mortality is difficult to ascertain as many of the neonatal illnesses have overlapping features. Causes of neonatal mortality are often misclassified [57]. As noted earlier, the neonatal mortality burden is largely concentrated in low- and middle-income countries which lack vital registries that can provide reliable data. Neonatal mortality data are often based on verbal autopsy, estimations, and surveys that are inherently riddled with high risk for inaccuracies [56-59]. However, the interventions to prevent the aforementioned complications when administered as a package of care have shown notable effectiveness in preventing neonatal mortality [25, 28, 30, 53-55].

Resuscitation

The majority of neonates who require resuscitation respond to simple interventions such as drying, stimulation, and bag and mask ventilation [39, 42-44]. Delay in providing basic resuscitation steps results in a rapid increase in the risk of mortality and morbidity [33]. The meta-analysis of studies on basic neonatal resuscitation in resource-limited settings shows a decrease in birth asphyxia/intrapartum-related deaths (RR= 0.70, 95% CI 0.59-0.84) [60] fresh stillbirth (RR 0.74, CI 0.61 to 0.90), neonatal (RR 0.58, 95% CI 0.42 to 0.82), and perinatal mortality (RR 0.82, 95% CI 0.74 to 0.91) [55]. It should be noted that the major focus of basic neonatal resuscitation guidelines for low- and middle-income countries has been on providing immediate drying, stimulation, maintaining open airway, and bag and mask ventilation [47, 48, 50]. NRP [15] and ILCOR[16] guidelines recommend the presence of two NRP trained providers as well as instruments and supplies like heart rate monitoring, saturation monitoring, oxygen source with blender, CPAP, laryngoscope, endotracheal tube, laryngeal mask, intubation supplies, umbilical line supplies, IV line supplies, epinephrine, normal saline and other medications. However, most neonates respond well to basic neonatal resuscitation which can be administered by a single provider with minimal equipment like bag-mask device, clean cloth, a sterile cord tie and blade/scissors [13, 47, 48, 50]. Neonatal resuscitation should be followed by basic neonatal care as described in Early Essential Newborn Care, Essential Care for Every Baby [51], and Essential Care for Small Babies [52] as applicable.

Prematurity

Prematurity-related complications is the leading contributor to neonatal mortality [7, 61]. The incidence of prematurity has been steadily increasing. In 2015, there were an estimated 15 million premature births and 1 million premature neonatal deaths [7, 61, 62]. Many premature neonates who survive suffer from long term complications. Prematurity-related neonatal deaths are concentrated in low- and middle-income countries. About 75% of the prematurity-related neonatal deaths and the majority of the morbidities can be prevented by implementing low-cost interventions like essential neonatal care, antenatal corticosteroids, kangaroo mother care and exclusive breastfeeding, and early identification and treatment of neonatal illnesses [61]. Antenatal corticosteroids have been proven to be effective in reducing several adverse outcomes in high-income countries. In a meta-analysis of studies conducted in high-income countries, antenatal corticosteroids decreased perinatal deaths (aRR 0.72, 95% CI 0.58 to 0.89), neonatal deaths (RR 0.69, 95% CI 0.59 to 0.81), respiratory distress syndrome (aRR 0.66, 95% CI 0.56 to 0.77), moderate/severe respiratory distress syndrome (aRR 0.59, 95% CI 0.38 to 0.91), intraventricular hemorrhage (aRR 0.55, 95% CI 0.40 to 0.76), necrotising enterocolitis (RR 0.50, 95% CI 0.32 to 0.78), need for mechanical ventilation (RR 0.68, 95% CI 0.56 to 0.84), and systemic infections in the first 48 hours after birth (RR 0.60, 95% CI 0.41 to 0.88) [63]. However, the large cluster-randomized trial conducted in low- and middle income countries of antenatal corticosteroids (ACT Trial, N= 4778) there was no benefit in neonatal mortality or any other major outcomes and suspected maternal infection increased in the intervention group (OR 1·67, 1·33-2·09, $p<0{\cdot}0001$) [64] The results of this study led to a cautious approach by WHO by restricting antenatal corticosteroids to hospital settings in women with high risk for preterm delivery between 24-34 weeks of gestation [61, 65, 66]. The WHO sponsored clinical trial of antenatal steroids in low- and middle-income countries (WHO ACTION Trials) will provide additional information on the impact of antenatal corticosteroids and neonatal maternal outcomes. Antenatal magnesium sulfate for preterm neuroprotection has not been studied in low and middle-income countries. Thus, although antenatal magnesium sulfate for preterm neuroprotection is a standard of care in high-income countries based on multiple trials and meta-analyses[67-71], it is not recommended by WHO to be used outside of hospital settings in low and middle-income countries [66]. WHO additionally recommends antenatal antibiotic treatment for preterm labor and surfactant therapy for treatment of infants intubated for respiratory distress syndrome that specifically take place in hospital settings [66].

Prematurity-related deaths continue to happen well beyond the immediate delivery and resuscitation period [72]. Therefore, it is important for healthcare providers to closely follow up preterm neonates for early identification of danger signs and referral [72, 73]. Mothers and immediate caregivers should be educated with programs such as Essential Care for Small Babies [52] and about identification of neonatal danger signs. Efforts should be made to strengthen local infrastructure to provide facility-based care for preterm neonates until they can be safely discharged to home in mother or family’s care as medical care to preterm neonates has a high impact on premature neonatal survival [73].

Sepsis and Infection Prevention

Sepsis contributes to about one third of neonatal mortality worldwide [7, 56]. About half of the sepsis-related deaths happen secondary to early-onset sepsis (within 3-7 days of life) and the rest is due to late-onset sepsis (>7days of life) [72]. [74]. Close attention should be paid to the antenatal/perinatal history and maternal high-risk factors for sepsis. [75]. Low birth weight and premature neonates are at 3-10 times higher risk for sepsis than term neonates because of limited host defenses, immune immaturity/dysfunction, and lack of transplacental maternal antibody transfer [75]. Neonatal care providers should be aware of the increased risk for sepsis in premature and low birth weight neonates, and a close follow-up of such neonates should be ensured.

It is important for the provider to educate the mother and the family about clean postnatal care practices as late onset sepsis accounts for about half of the sepsis related neonatal mortality. In a systematic review on the effect of various practices on neonatal mortality, it was found that there was a significant reduction in neonatal mortality with resuscitation provider handwashing (19%, 95% C.I. 1-34%), maternal handwashing (44%, 95% C.I. 18-62%), clean delivery practices (at home (15% , IQR 10-20%) or in a facility (27%, IQR 24-36)), and clean postnatal practices (40%, IQR 25-50%) [76]. There have been studies from different parts of the world indicating the wide scale prevalence of harmful postnatal care practices which predispose the neonates to the risk of sepsis [77-81]. Neonatal sepsis secondary to harmful cultural practices is an area with considerable scope for providing population-based educational initiatives. In addition to education about neonatal care practices, population-based initiatives should also be targeted for education regarding early identification of neonatal sepsis signs. Close follow-up of all neonates, especially the ones with risk factors for sepsis should be done to facilitate early identification, prompt treatment, and referral of sick neonates [72, 73].

Prevention of Hypothermia

As neonates have limited capacity to thermoregulate, normothermia is critical for neonatal survival [82]. The transition from the fetal environment to the extrauterine environment is associated with marked thermodynamic changes which can result in hypothermia unless active efforts are made to prevent it [83]. As their immature thermoregulatory mechanisms get easily overwhelmed, hypothermia is especially dangerous to premature and low birth weight neonates and it can rapidly result in multisystem compromise if left untreated [84]. Additionally, neonates with growth restriction, asphyxia, feeding difficulties, and hypoglycemia are also at increased risk of hypothermia and related complications [85]. Neonatal hypothermia can lead to multisystem symptoms like breathing difficulty, feeding difficulty, lethargy, and shock. Moreover, neonatal hypothermia has been shown to be independently associated with increased risk of mortality, intraventricular hemorrhage, respiratory diseases, hypoglycemia and late-onset sepsis [86]. Therefore, it is difficult to attribute the possible impact on neonatal mortality to hypothermia. In a meta-analysis of observational studies, the reported hypothermia incidence was found to be very high (as high as 90% in a few studies from low and middle-income countries) [85]. Neonatal hypothermia-related case fatality rates have been described in the range from 8.5% to 80% with fatality rates increasing proportionally to the degree of hypothermia [85, 87-89] Prevention of hypothermia is one of the first and most important interventions for ensuring the optimal neonatal outcome. Care should be taken to ensure that the delivery room is > 25*C[90]. Immediate drying and early skin to skin care by placing the neonate on mother’s chest should be ensured [13, 48, 50-52]. Additionally, caps, plastic wraps, infant radiant warmers, and exothermic mattress should be used whenever necessary and feasible [90-94].

Delayed cord clamping

Delayed cord clamping is a simple intervention that provides benefits for term [95, 96] and preterm neonates [97-100]. In term neonates, delayed cord clamping has been shown to increase the neonatal iron stores and about 50% decrease in the risk for subsequent anemia [95, 96]. In preterm neonates, there is a decrease in mortality, anemia, blood transfusion requirement, hemodynamic instability, IVH, and necrotizing enterocolitis [97-100]. Delayed cord clamping may improve neurodevelopmental outcomes [101, 102]. As delayed cord clamping is an inexpensive and easy to administer intervention, it has been recommended in all neonatal resuscitation guidelines since 2010 [13, 15, 16, 47, 48, 50].

Early and Continued Skin to Skin Care

Skin to skin care immediately after birth has also been advocated continuously in neonatal resuscitation guidelines for low- and middle-income countries [13, 45, 48, 50-52]. Early skin to skin care immediately after birth promotes better thermoregulation in neonates and significantly decreases the chances of hypothermia [103-105]. Early skin to skin care enhances cardiorespiratory stability and decreases the incidence of hypoglycemia [106, 107]. Early skin to skin care decreases the time taken to initiate breastfeeding, increases the breast milk supply, increases the chances of exclusive breastfeeding and breastfeeding duration [106-110]. Early skin to skin care decreases maternal pain due to episiotomy, pain during the third stage of labor and also decreases the duration of the third stage of labor [105, 108]. Early skin to skin care increases maternal satisfaction and mother-infant bonding [110]. Skin to skin care continued beyond the immediate delivery period offers important benefits to the neonate including decrease in neonatal mortality and morbidity rates, decrease in rates of serious infection, increasing rates of exclusive breastfeeding, improving neonatal growth, decreasing hospital admission rates, improving maternal satisfaction, improving maternal-infant bonding and improving maternal competence [111-115]. The benefits of neonatal skin to skin care are particularly remarkable for preterm and low birth weight neonates [111, 113-115]. Skin to skin care should be given to all neonates following birth. Mothers and other care providers should be encouraged to continue skin to skin care as long as feasible.

Future directions

Unattended home deliveries and deliveries that are attended by untrained birth attendants continue to be painfully frequent in low- and middle-income countries [18, 36-38, 116-118]. Many health care facilities in low- and middle-income countries are poorly equipped and staffed to provide adequate neonatal care [18, 119, 120]. Serious and sustained efforts are required to fill these life-threatening gaps in neonatal care. Institutional delivery should be promoted wherever feasible. Where home delivery is the only option, it should be made sure that a trained birth attendant is present for every delivery as perinatal mortality can be decreased with adequate training [121]. Several studies have shown that the competence of trained birth attendants decreases over time [122-124] so continued efforts should be made for retraining of traditional birth attendants to ensure optimal competency [123-126]. Individualized neonatal referral and emergency preparedness plans should be crafted for each village/cluster, and health providers should receive training in how to deal with common neonatal emergencies including prompt and safe neonatal transport. Transport networks and transport infrastructure (teams, ambulances, triage helpline) connecting community-level health centers to tertiary health centers should be devised for individual regions. Health promotion and neonatal care education during the antenatal period and post-natal period should be strengthened. As neonatal deaths continue to happen well beyond the immediate post-delivery period [72, 73], follow up of all neonates and a close follow-up of at-risk neonates once or twice during the first week should be ensured. This would also provide an educational opportunity to reinforce components of essential newborn care and early identification of danger signs as well as identify and educate care providers about harmful neonatal care practices. Community-level education about essential newborn care, neonatal care practices, and early identification of neonatal danger signs should be implemented to raise mass awareness.

Last but not least, antenatal care including antenatal screening should be strengthened to identify high risk pregnancies and neonates with congenital anomalies during the antenatal period. Screening for maternal hypertension/pre-eclampsia and diabetes should be conducted. Identification and management of preterm labor is essential. Congenital anomalies contribute to about 11.3% [7, 56] of total neonatal mortality. Currently, there seems to be little effort by neonatal health policymakers regarding tackling neonatal mortality burden associated with congenital anomalies. Delayed recognition of congenital anomalies precludes optimal planning and referral of neonates with these conditions.

Conclusions

Although remarkable progress has been made in neonatal care in low- and middle-income countries, much remains to be achieved. Low- and middle-income countries continue to contribute disproportionally to neonatal mortality. Simple and inexpensive interventions like prompt and effective basic resuscitation, clean delivery and handwashing by care providers, early and exclusive breastfeeding, essential care for preterm and small babies, early and continued skin to skin care, ensuring normothermia, and delayed cord clamping are critical for improving neonatal outcomes in low- and middle-income countries. Key preventative neonatal care interventions such as mother and family education about essential newborn care, education about danger signs, early follow up of all neonates and closer follow up of at-risk neonates should be ensured. Anticipation and early identification of neonatal illness with a prompt transfer to a higher care center is essential for the survival of sick neonates.

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Figure Legend:

Figure 1 Helping Babies Breathe Second Edition Action Plan

Abbreviations: ECEB, Essential Care for Every Baby; HMS, Helping Mothers Survive.

Source: Niermeyer S, Kamath-Rayne B, Keenan W, Little G, Singhal N, Visick M, eds. (2016).7

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Figure 2 Difference Original Calibration-Revised Calibration

Table 1. Neonatal care guidelines for low and middle-income countries

Guideline	Antenatal education	Delayed Cord Clamping	Skin to skin care	Resuscitation	Early breast feeding	Prematurity	Infection prevention Clean delivery practices	Follow up	Newborn care education including danger signs
Essential Newborn Care (ENC), WHO, 1994 [45]			+	+	+	+	+		+
Basic Newborn Resuscitation, WHO, 1998 [46]				+			+		
Helping Babies Breathe (HBB), AAP, 2010 [13]		+	+	+	+		+		
Basic Neonatal Resuscitation, WHO, 2012 [47]		+		+					
Early essential newborn care guidelines, WHO, 2014 [48]	+	+	+	+	+	+	+	+	+
Essential Care for Every Baby (ECEB), AAP, 2014 [51]			+		+	+	+	+	+

Timeline and components of major neonatal care guidelines for low- and middle-income countries, + indicates that the intervention was present in the guideline. WHO= World Health Organization, AAP= American Academy of Pediatrics

Second Edition

ACTION PLAN

Helping Babies Breathe

Prepare for birth*

See HMS Action Plans for mother

Birth

Dry thoroughly

Crying?

Crying

Not crying

Keep warm
Clear airway if needed
Stimulate

Breathing?

Breathing well

Not breathing

Keep warm
Check breathing

Ventilate
Cut cord

Breathing

Cut cord

Not breathing
No chest movement

Call for help

Monitor
with mother

Essential Care for Every Baby
(See ECEB Action Plan)

Improve ventilation

Breathing

Not breathing

Heart rate?

Normal

Not
breathing

Slow

Continue ventilation
Decide on advanced care

The Golden Minute®

60 sec

*Equipment to help a baby breathe

- Gloves
- Cloths
- Head covering
- Scissors
- Ties /Clamps
- Suction device
- Ventilation bag-mask
- Stethoscope
- Timer (clock, watch)

Disinfect equipment immediately after use

Helping Babies Breathe®
THE GOLDEN MINUTE®

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

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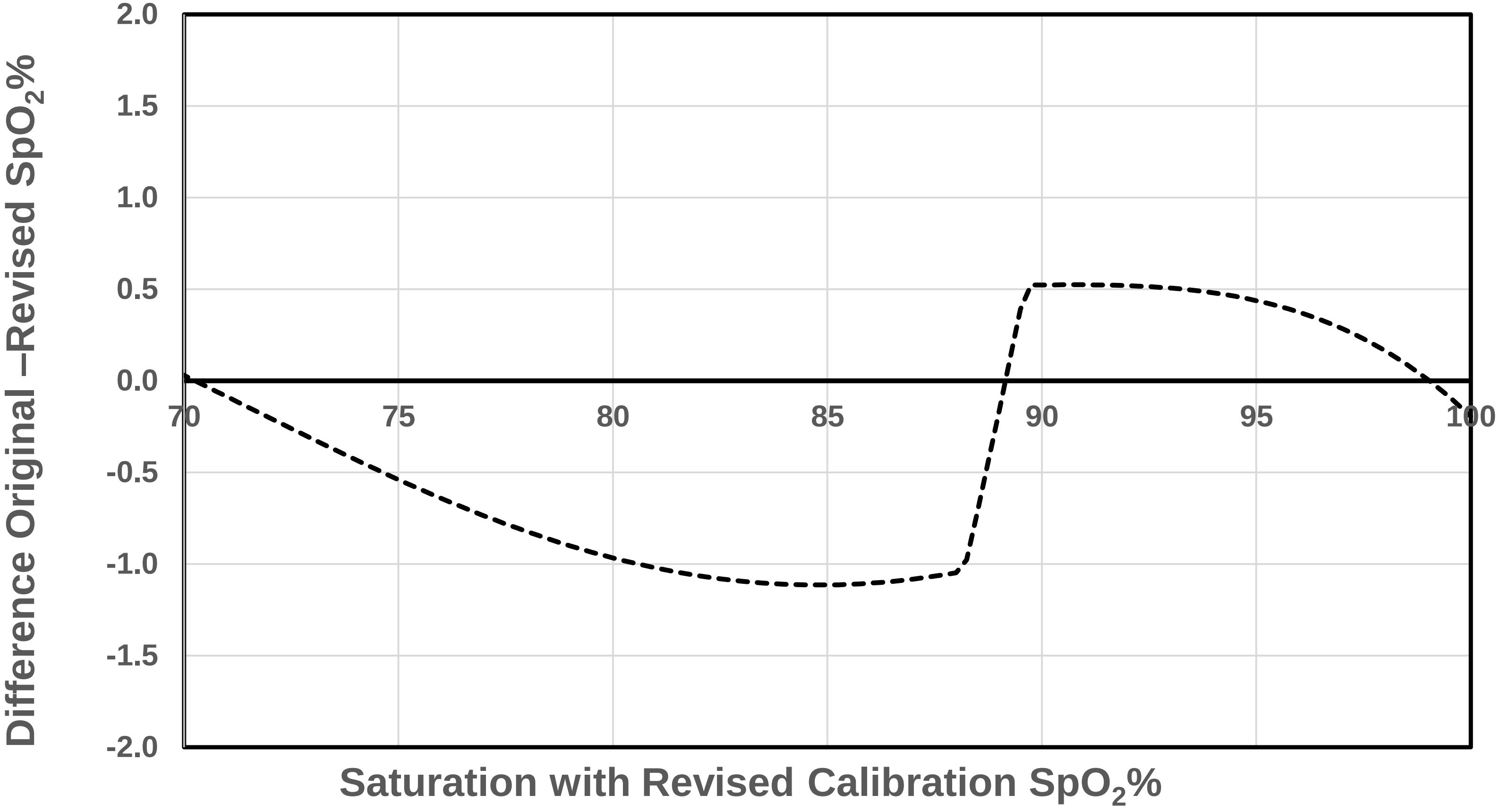

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Ethics and Medico-legal implications in delivery room emergencies

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ABSTRACT

There is very little law-either case law or statutory law - that regulates delivery room decisions about resuscitation of critically ill newborns. Most of the case law that exists is decades old. Thus, physicians cannot look to the law for much guidance about what is permissible or prohibited. Local hospital policies and professional society statements provide some guidance, but they cannot be all-inclusive and encompass all potentially encountered scenarios. Ultimately, the physician, the medical team, and the parents must try to reach a shared decision about the best course of action for each individual infant and each unique family. In this paper, we review some of the case law that may be applicable to such decisions and make recommendations about how decisions should be made.

Imagine for a moment you are a neonatologist taking overnight, in-house call at your community delivery hospital. You are paged urgently at 0200. A woman has presented at 22 and 5/7 weeks gestation, fully dilated, with a bulging bag of water. The mother was late in seeking prenatal care and is uncertain about her dates. She speaks only Spanish. You do not speak Spanish. One of the labor and delivery nurses, whose Spanish is clearly rudimentary, is trying to translate. The certified interpreter has been called but has not yet responded.

The woman is writhing in pain.

You and the obstetricians have to make some quick decisions. Clearly, this is not an ideal circumstance for her to make an informed decision regarding her wishes in the resuscitation of her “soon to be delivered” extremely premature baby.

What do you, as the neonatologist, do once the baby is born? Do you initiate intensive resuscitative efforts? Provide comfort measures only? If you choose to resuscitate, how far do you go? Chest compressions? Epinephrine? What if you decide upon comfort care, and you tell that to the patient as best you can, and she gives what seems like tentative approval, and then the infant appears more mature than 22 weeks? If you go against parental wishes, could there be legal ramifications?

While delivery rooms are typically a venue for joyous celebrations of the miracle of life, they are, unfortunately, also a place where doctors face emergency situations and ethical dilemmas for which they must make immediate decisions. In this review, we will examine some of the most commonly encountered delivery room emergencies. These arise following deliveries at the limits of viability, when infants have significant congenital anomalies, and when there is a non-reassuring fetal heart rhythm and subsequent concern for hypoxic ischemic encephalopathy. We will review landmark legal cases and describe ethical principles that may assist in decision making.

1. The borderline of viability

Of the 3.86 million births in the United States in 2017, nearly 26,000 infants were born extremely premature ($<$ 28 weeks gestation) [1], with a smaller subset between 22 and 24 weeks gestation-the “Gray Zone” of viability. The American Academy of Pediatrics (AAP), The American College of Obstetrics and Gynecology (ACOG) and other governing bodies agree that, to some extent, parental wishes should guide decisions regarding the extent of resuscitative efforts afforded to infants born within this uncertain periviable state [2]. [3]. Sometimes the medical team has the time and opportunity to adequately counsel parents so that they can make an informed decision as to what they feel is in the best interest of their child. At other times, imminent delivery, pain, extreme emotion, language/educational barriers, provider bias, and other factors may hinder ideal counseling. Sometimes the medical team and family may agree regarding how best to proceed at the time of delivery. Other times viewpoints may be in opposition. One of the most well-known legal cases surrounding resuscitation at the limits of viability is that of *Miller v. HCA*. [4].

In August of 1990, Sidney Miller was born at 23,1/7 weeks gestation, weighing 615 g. Sidney's mother, Karla, had presented in preterm labor to Woman's Hospital of Texas. After receiving counseling by the physician team, she and her husband, Mark, decided that they did not wish to pursue heroic measures for their daughter. Thereafter, the leadership of the hospital met, and decided that a hospital policy required resuscitation for any infant $>$ 500 g. (It was later determined that such a policy did not exist.). By that policy, a neonatologist must be present at the time of delivery, assess the gestational age and weight, and decide whether or not to proceed with resuscitation. When informed of the hospital's policy and decision, Mark refused to sign a consent form and asked what could be done to prevent resuscitation

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attempts. The only choice given was for his ill wife to leave the hospital.

Approximately 11 h later, Sidney entered the world. She was cyanotic, limp, and bradycardic. She cried spontaneously in the delivery room. She received bag-mask-ventilation and was intubated. Apgar scores were 3 at 1 min and 6 at 10 min. The neonatal fellow stated that he decided to proceed with resuscitative efforts “because this baby is alive, and this is a baby that has a reasonable chance of living.” Even though the parents had previously stated that they did not want resuscitation, they apparently did not object, in the delivery room or the NICU, to Sidney's treatment after birth. Early in Sidney's NICU course, she had a severe intracranial hemorrhage. This resulted in long-term sequela. By the time Sidney was seven years old, according to court records, she “could not walk, talk, feed herself, or sit up on her own. [She] was legally blind, suffered from mental retardation, cerebral palsy, seizures, and spastic quadriparesis in her limbs. She could not be toilet-trained and required a shunt in her brain to drain fluids that accumulate there and needed care 24 h a day. The evidence further demonstrated that her circumstances will not change.” [4].

The Millers filed a lawsuit against Woman's Hospital of Texas and its parent cooperation Columbia/HC Healthcare Corporation (HCA) alleging battery and negligence in the resuscitation of their daughter. The couple did not name any individual physicians in the lawsuit. In the original trial, the jury sided with Millers, awarding a $60 million dollar verdict, which included $13,500,000 in punitive damages, designed to serve as a warning to other institutions should they proceed with similar actions. The verdict was appealed to the 14th District Texas Court of Appeals which overturned the lower court's verdict in a 2-1 decision.

The Court of Appeals based its reversal on their interpretation of the Texas Natural Death Act. By that interpretation, parents are only legally authorized to withhold medical treatment for a child if the child's condition has been determined to be “terminal.” While a court order is generally required to override parental refusal of treatment, such an order was deemed unnecessary when a physician faced an urgent need for life-sustaining treatment of a child who was not terminally ill. This ruling was then appealed up to the Texas Supreme Court.

The Texas Supreme Court appropriately summarized what was being asked of them in *Miller v. HCA* by stating “This case requires us to determine the respective roles that parents and health care providers play in deciding whether to treat an infant who is born alive but in distress and is so premature that despite advancements in neonatal care, has a largely uncertain prognosis.” [4].

Prognostic uncertainty is one of the fundamental issues impacting decision making for infants at the limits of viability. Nowadays, approximately 38% of infants born at 23 weeks gestation and admitted to a neonatal intensive care unit will survive and around 35% of survivor will have no significant neurologic impairment [5]. While population statistics provide clinicians with a starting point for prognostication, they provide much less assistance in determining if an individual infant will be one of the survivors. Factors such as birth weight, antenatal corticosteroid use, sex, and a singleton pregnancy can influence survivability and parental counseling, but these factors still provide little in the way of certainty for any individual infant [6]. Significant long-term morbidity and neurologic impairment is influenced substantially by complications endured during the neonatal course, (i.e the intracranial hemorrhage sustained by Sidney Miller), and this information will clearly be unavailable to the physician at the time of prenatal counseling. If a clinician could say with certainty that an individual infant will be survivor and a survivor without significant impairment, it would make it much easier to determine rather or not it is appropriate to override parental authority. All good ethics begins with good facts, and unfortunately at the limits of viability the facts remain murky.

Ultimately, the Texas Supreme Court upheld the 14th District Court's ruling and the $60 million verdict was negated. The Millers were awarded nothing. Citing a case from 1920, the court ruled that under emergent circumstances a physician may provide life sustaining treatment without obtaining parental consent. Further, they ruled that, in a case of extreme prematurity, a decision about resuscitation could not be made prior to birth. The ruling sparked controversy in the legal, medical and ethics communities alike. While this decision gives wide latitude to the physician under emergent circumstances and sets the precedent that the delivery of a periviable infant will always be an emergency, it has no impact on the role of parental authority in non-emergent circumstances. Should the Millers have requested to have life sustaining therapies discontinued following Sidney's intracranial hemorrhage, they would have maintained the parental authority to do so and the medical team likely would have been supportive of such a request. In essence, doctors in the delivery room are playing the odds. While it is impossible to know for certain, it seems likely that the Millers would not have pursued legal action if Sidney's neurological outcome had been better.

In a 2004 New England Journal of Medicine article, George Annas made the claim that even though Sidney Miller's birth took place back in 1990, “nothing has changed in the practice of neonatal medicine since then that would prevent repetition today.” [7] Fifteen years later, this likely still holds true. Through the currently adopted shared decision-making model, when outcomes are uncertain (falling within the “gray zone”) parental values should determine what decision is made [8]. By that approach, the Miller's decision should have been respected. Nevertheless, sometimes doctors override parents' requests. Babies in the same circumstances as Sidney Miller might still be resuscitated today. The Miller decision is one case decided by one state's judicial system. In a different case, courts might decide differently.

From a legal perspective, the most important thing would seem to be for a hospital to have a policy dictating its approach to these decisions and for each hospital to follow its own policy. That clearly leads to different approaches at different hospitals. Rysavy and colleagues recently showed that, for babies born at 22 weeks of gestation, some hospitals resuscitate all such babies, some resuscitate some, and some resuscitate none [9]. Remarkably, these variations in hospital practice have not led to litigation. Clearly, there is no hard and fast legal rule about resuscitation decisions at the borderline of viability.

2. Congenital anomalies

Approximately 3% of all infants born in the United States each year have a major structural or genetic birth defect [10]. Luckily, many of these anomalies (i.e. cleft lip, club foot) do not impact delivery room management or long term survival. Nonetheless, a smaller portion of birth difference can greatly influence initial neonatal management. Dilemmas arise particularly when the anomaly was unknown prenatally and there are multiple malformations. The presence of, or suspicion for, an underlying genetic syndrome may also influence decision making and parental counseling. The Baby Doe case and subsequent regulations have impacted decision making for infants with congenital anomalies and genetic syndromes.

In 1982 in Bloomington, Indiana an infant, “Baby Doe” was born with Down Syndrome and a tracheoesophageal fistula. The parents and the medical team decided it was in the infant's best interest not to proceed with surgical interventions and to withhold parenteral nutrition. The infant was prescribed morphine and phenobarbital for pain and restlessness [11]. The family physician and a local pediatrician disagreed with the plans and sought legal and adoption resources. An Indiana court deferred to the parental authority and ruled that the baby should be given comfort care only, in line with the parental wishes. The verdict was appealed to the Indiana Supreme Court. While awaiting a ruling, the infant died at six days of life. General C. Everett Koop was Surgeon General at the time and was outraged by the situation. He cited a nearly 100% success rate with tracheoesophageal fistula in his own experience at Children's Hospital of Philadelphia and felt the decision made to forgo treatment was made only on the basis of the diagnosis of Down Syndrome and was thus discriminatory [12].

While the Baby Doe case itself did not unfold in the delivery room, the subsequent Baby Doe regulations issued by The Department of Health and Human Services (DHHS) had implications for delivery room management. Under these regulations, based on section 504 of the Rehabilitation Act of 1973, federal funding could be withheld from any organization not complying with the Baby Doe rules. DHHS initially mandated that posters be displayed in all delivery rooms, nurseries and maternity wards that stated, “Discriminatory failure to feed or care for handicapped infants in this facility is prohibited by federal law.” [13] A toll free number was included to report violations to the Infant Doe Hotline. Then Secretary Richard Schweiker stated, “The President has instructed me to make absolutely clear to health care providers in this nation that federal law does not allow medical discrimination against handicapped infants.” [14].

The Baby Doe policy stirred political, legal, ethical and medical debate and the American Academy of Pediatrics amongst others brought suit against the DHHS. US District Court Judge Gerhard Gesell found the regulation invalid. DHHS made minor modifications, reissued the rules, and opened the proposed rules for a 60 day comment period. Of the 16,739 comments DHHS received, 97.5% were classified as supportive, yet 72% of pediatricians opposed the regulations [14]. Opponents believed that the regulation provided no useful guidance to physicians but only frightened them into over treating at the potential expense of increased suffering.

It wasn't long before the Baby Doe rules were tested judicially. On October 11, 1983 an infant known as Baby Jane Doe was born in New York with spina bifida, hydrocephalus, kidney damage and microcephaly [15]. Her parents were counseled that she would be paralyzed below the levels of the lesion, severely retarded and prone to frequent urinary tract infections. The physician team disagreed and argued that surgical interventions and intensive treatment was appropriate for the infant. The parents felt that palliative care was in their child's best interest. The case found its way to the courts and was appealed up to the level of the US Supreme Court.

In *Bowen v American Hospital Association* the Supreme Court struck down the federal regulations [16]. They endorsed the best interest standard stating that “concerned and loving parents had chosen one appropriate medical course over another and made an informed decision in the best interest of the infant.” The legal decision supported parental rights, but the societal controversy changed the landscape of decision making forever [17]. [18] While the legal precedent of the Baby Doe case would suggest that parents have the right to refuse surgery for a baby with Down Syndrome and a correctable surgical anomaly, it seems unlikely that a future court would take the same stance.

Medical ethics always finds itself at the crossroads of societal views and cultural norms, legal and political influence, and medical advancements and knowledge. Thus, positions can shift overtime. While in 1982, granting parental authority to decline a straightforward surgery simply because the infant had Trisomy 21 may have been ethically permissible, nowadays it almost certainly is not. Today, treatment decisions for an infant with Trisomy 18 (and to a lesser extent Trisomy 13) have moved from the zone of futility into the gray zone of parental discretion [19].

One could speculate that, in the not too distant future, medical knowledge and societal values may change yet again and interventions for infants with Trisomy 18 may become defined as clearly beneficial and therefore once again outside the allowed realm of parental discretion. As technology advances and our understanding of genomic medicine continues to improve, the potential for genetic discrimination could become even more relevant.

If there were not a Baby Doe, would there be a Sidney Miller? Certainly one could argue that the culture and climate created by the Baby Doe regulations could have played a role in Women's Hospital of Texas's feeling that they were required to resuscitate Sydney Miller. When asked about his through on the *Miller v HCA*, General C. Everett Koop responded “I don't think parents should have the discretion to kill their children. I'm a great believer in the slippery slope. You get into the terrible quagmire of having only perfect children, and nobody can guarantee that.” [20].

3. Hypoxic ischemic encephalopathy

When labor is progressing expectantly and then, suddenly, fetal heart monitoring reveals decelerations and fetal bradycardia, there is a true delivery room emergency. Such emergencies also arise when there is placental abruption, umbilical cord prolapse, or uterine rupture. In such cases, since two patients' lives are at stake, the actions of two different medical teams, obstetrics and neonatology, must be coordinated and mobilized rapidly. When newborns are born depressed, life saving interventions must be initiated rapidly. However, when infants fail to respond to medical interventions, the potential for devastating neurologic sequelae must be considered and clinicians are faced with the difficult decision of when and if it is in the infant's best interest to cease resuscitative efforts. Unfortunately, this scenario and these cases have been a frequent target for medical malpractice claims. Of the top 10 pediatric malpractice claims, the brain-damaged infant tops the list and has an average payout of $524,047 per case [21].

Emotional responses tend to be more raw and more intense in cases of unanticipated delivery room emergencies than in situations where there has been a prenatal diagnosis. The family has likely lived in a state of naive bliss, anticipating a delivery at term in which everything will be fine. And then suddenly it isn't fine. There has been no warning of trouble, no time to prepare. Adding insult to injury, many cases lead to an emergent cesarean section, with the mother under general anesthesia. Obviously, this greatly inhibits the ability to communicate effectively with the family. The mother cannot be updated on the infant's clinical response to interventions and the clinician is unable to elicit her views and wishes. Perhaps one of the worst tasks in the job description of a neonatologist is telling a mother who has just awoken from general anesthesia that her baby has died.

Guidelines from the American Heart Association and the Neonatal Resuscitation Program state “An Apgar score of 0 at 10 min is a strong predictor of mortality and morbidity in late preterm and term infants. We suggest that, in infants with an Apgar score of 0 after 10 min of resuscitation, if the heart rate remains undetectable, it may be reasonable to stop assisted ventilation; however, the decision to continue or discontinue resuscitative efforts must be individualized [22].” The language is left intentionally vague and ambiguous, as variables such as the quality of resuscitation, availability of therapeutic hypothermia, circumstances prior to delivery and family wishes should be taken into account. The recommendation is based on analysis of 6 studies, deemed very-low-quality evidence, that report a collective 42% survival at 22 months of age for infants > 36 weeks gestational age with an Apgar scores of 0 or 1 for > 10 min. Looking specifically at the 3 studies performed after 2009, when therapeutic hypothermia was available, of the 56 cooled infants, 27% survived without major/moderate disabilities [23]. The recommendation was opened for public comment and generated much discussion and debate. The group felt that the decision to continue or discontinue resuscitation efforts should be based on consultation with the family, but they also felt that parents tend to choose continuation even when data are presented. Thus, as in cases of periviability and congenital anomalies, clinicians are left in the gray zone of parental discretion and clinical uncertainty.

4. Conclusion

The seventh edition of the Textbook of Neonatal Resuscitation states, “There is currently no federal law in the United States mandating delivery room resuscitation in all circumstances … In most circumstances, it is ethically and legally acceptable to withhold or withdraw resuscitation efforts if the parents and health care providers agrees that further medical intervention would be futile, would merely prolong

Table 1

1. **Be okay with the gray.** Complex decisions deserve complex individualized analysis for each case and scenario. Attempting to create broad, overreaching, black-and-white guidelines for all extremely premature infants is taking the easy way out. Decisions about infants at the borderline of viability must enter into the gray zone, so proper due diligence regarding decision-making is awarded to the tiniest of humans. This means, however, that the treatment plan for the infant born to a mother in preterm labor at 23 weeks might not be decided before the baby is born. It also means that two 22 5/7 week gestation infants born on the same day, but with different characteristics, might not be managed in exactly the same way. That's okay.
2. **Do not place too much emphasis on gestational age.** If every fetus came with a stamped 'conceived on' date, then gestational age might carry a bit more weight. Given the imprecision of dating methods at up to ± 2 weeks, the utility of gestational age decreases substantially. Even if every infant was conceived by artificial methods and gestational ages were exact, other factors greatly impact both survival and long-term outcomes.
3. **Dying is usually not in an infant's best interest** – at least not right away. Whereas long term outcomes, QOL, and the burden of care are clearly important, if the infant is not allowed a 'trial of life', s/he will never have the opportunity to confront these future obstacles in care. It is hard to argue that death without a proper chance at life is ever in the best interest of an infant.
4. **Impairment does not necessarily equal poor QOL.** To high functioning adults, the thought of being blind, deaf, or having any degree of cognitive impairment would easily equate to a poor QOL. However, as former 'preemies' and ELBW infants reach young adulthood, their self-reported QOL scores equal those of their normal birth weight counterparts. Perhaps there is an element of blissful ignorance or denial, but this goes to show that one cannot be the judge of someone else's QOL.
5. **Just because the train has left the station doesn't mean you can't get off.** Just because the decision was made to attempt resuscitation at 23 weeks in the delivery room, it does not mean that the baby is automatically committed to a tracheostomy, gastrostomy tube, and home ventilator at the age of 6 months. Discussions about the care of extremely preterm infants must be ongoing. Parents and the medical team are welcome to alter the course of treatment at any time, should complications arise. It must be remembered that withdrawal of care is ethically equivalent to the withholding of care.
6. **Respect powerful emotions. They reveal moral truths.** It is clear that parents serve as the best surrogate decision-makers for an extremely premature infant (at least most of the time anyway). They should be appropriately informed about what the infant may endure, and they should play an active role in decision-making. However, not all the burden should fall on the parents. It is appropriate for the medical team to be somewhat directive. Making the decision to resuscitate an infant at the borderline of viability is not the same as obtaining informed consent prior to a surgical procedure and should not be met with the same rigor. Childbirth is a highly emotionally charged event and typically there is not the luxury of time. Even if all available outcome data were eloquently described to parents in the most dismal of settings, it is still quite likely the parents would request to have 'everything' done. Emotion and feelings of parental duty will overrule logic without direction and guidance from the medical team.
7. **Be aware of the self-fulfilling prophecy.** Several of the available policies and practice guidelines cite low survival rates as the premise for not recommending resuscitation at 22 weeks' gestation. If resuscitation is never attempted at 22 weeks, then of course no infants will survive at 22 weeks, adding merit to the original recommendation. Thus, a self-fulfilling prophecy is created. This may or may not explain the increased survival rates seen in the Japanese population and should be considered when making decisions about infants at the borderline of viability. In the 1950s, the survival rate at 26 weeks was close to zero, because resuscitation was not even attempted. Today, it is > 80%. Granted, size and state of embryologic development likely play a greater role at 22 weeks.
8. **Time lag likely skews all outcome data.** An infant admitted to a NICU today does not receive the same care as an infant born in 1995, or even in 2013 for that matter. By the time data can be collected, analyzed and published, advances in neonatal care undoubtedly will have occurred. Progress in neonatal care may not be as dramatic today as it was in the second half of the 20th century, but nonetheless long-term follow-up data must be interpreted cautiously when applied to an infant born today.
9. **Statistics can be both confused and confusing.** Available outcome studies and calculators describe population statistics but do not predict the individual outcome for a specific infant. A father could be told that 26% of infants born at 23 weeks' gestation survive, but there is no way to predict whether his daughter will be one of the 26 of the 100 who survive. For parents, ultimately statistics become an all-or-none retrospective phenomenon. If their child lives, survival is 100%. If their child dies, survival is zero. There is no such thing as 26% survival for an individual baby.
10. **Above all, never abandon parents.** Parents of babies in the NICU are on an emotional roller-coaster. They may behave badly. Some get angry. Some don't visit their babies. Others can be intrusive or critical of staff. Parents need the support and guidance of doctors and nurses. The parents who are the most difficult to get along with are often the ones who need support the most.

dying, or would not offer sufficient benefit to justify the burdens imposed on the baby." [24] Remarkably, there is very little case law and no statutory law that regulates or governs delivery room decisions. Thus, for good or bad, physicians are left with a lot of discretion. Local hospital policies should provide guidance and following hospital policy is always a good legal defense. But policies cannot be all-inclusive and encompass all potentially encountered scenarios. Ultimately, the physician and the medical team must simply do what they feel is best for infants based on their clinical judgment. They must use their experience and knowledge to decide what seems to be the best course of action for each individual infant. The decisions are often made in the split seconds allowed by medical emergencies.

In 2015, we offered ten suggestions for assistance with decision making at the limits of viability [25]. Many of these suggestions apply to emergency room deliveries as well (Table 1).

Physician vow to first do no harm. But it may be difficult to decide how to define "harm" in the setting of an emergent delivery with a vulnerable infant who will certainly die without intervention, whose future is radically uncertain, and for whom any choice might lead to harm. Letting a baby die who might have survived is one sort of harm. But it may not be the worst harm. Attempting resuscitation when resuscitation seems futile is another sort of harm. Much of the time in delivery room emergencies the line between futility and harm remains blurry and gray. Often, the best course is to provide immediate stabilization in order to allow for additional time to gather prognostic information and to facilitate further conversations with families. Delivery room decisions are not irreversible. If life-sustaining treatment is initiated in the delivery room, and the baby does not do well or the family wishes to withdraw life support later, then it is permissible, in some circumstances, to withdraw life support. Withholding life support initially or withdrawing it later are legally and ethically equivalent decisions [26]. Each baby is different. Each case needs to be evaluated individually. There are no hard and fast, black and white rules (either ethically or legally) for babies born at the borderline of viability. Thus, communication with parents and colleagues remains evermore essential.

Practice points

Do not place too much emphasis on gestational age. It is both inexact and an imperfect predictor of prognosis. Evaluate each infant as if you don't know the gestational age.

Impairment does not necessarily equal poor QOL. The self-reported quality of life of individuals with disabilities equals those of their non-disabled peers.

Discussions about the care of extremely preterm infants must be ongoing. Parents and the medical team may alter the course of treatment at anytime. Withdrawal of treatment is ethically and legally equivalent to the withholding of treatment.

Statistics can be both confused and confusing. The same statistics can reveal that "90% of babies born with Condition X either die or survive with severe disabilities" and that "50% of survivors with Condition X have no disabilities." Presenting statistics always requires choices about how to frame and explain the data.

Never abandon parents. Parents of babies in the NICU are on an emotional roller-coaster. They may behave badly, get angry, not visit their babies, or criticize staff. They all need the ongoing support and guidance of doctors, nurses and social workers.

Research Agenda

Why do significant practice variations exist in delivery room decisions?

What is the optimum way to engage parents in a process of shared decision making?

Conflicts of interest

Jessica Brunkhorst has no conflicts of interest to disclose.

John D. Lantos has no conflicts of interest to disclose.

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